

EPA Registration Jacket 43813-27

Vol. 2

Meeting Report

Subject: ECONEA Ecotoxicology

Date: March 29, 2005

Attendees:	Dennis Edwards (DE)	EPA
	Karen Leavy-Monk (KLM)	EPA
	Nader Elkassabany	EPA
	Jim Breithaupt (JB)	EPA
	Siroos Mostaghimi	EPA
	Norm Cook	EPA
	Kathryn Montague	EPA
	Richard Petrie	EPA
	Bill Goodwine (BG)	Janssen
	Piet Blancquaert	Janssen

1. BG summarized the existing data and provided an update on repeat and new studies requested by EPA. Rationale was reviewed pertaining to Janssen's waiver request on a number of studies for secondary metabolite CL322248 and an acute avian LC50 (mallard duck) toxicity study with primary metabolite CL322250. Additionally, Janssen requested that 2 aquatic toxicity tests be reconsidered. Since the presentation was provided in advance of the meeting, this went fairly quickly, allowing most of the time for discussion on certain key issues (i.e. BCF studies).
2. Currently available studies on both metabolites CL322250 and CL322248 indicate that the toxicity of CL322248 is the same as or less toxic than CL322248. Therefore Janssen proposed that EPA use the data for CL322250 in screening level risk assessments for the secondary metabolite CL322248.
3. Because of the potentially widespread use of the product, EPA is concerned about bioaccumulation of the parent or primary metabolite CL322250. Janssen is prepared to further study the potential for bioaccumulation in fish with the parent molecule R107894, however, a number of technical issues require further guidance from EPA. Janssen believes that the potential for bioaccumulation for both compounds is low based on the low $P_{o/w}$ for CL322250 (1.00 at pH 7 and 0.55 at pH 8), and the calculated theoretical bioconcentration factor for R107894 of 105. R 107894, which is toxic to aquatic organisms, hydrolyses rapidly in water ($T_{1/2}$ of 8 hours in fresh water, 3 hours in salt water).
4. According to OPPTS guidelines for bioaccumulation studies, the active substance needs to be tested at 1/100 and 1/1000 of the LC_{50} . Because of the low concentrations, it is technically impossible to have an acceptable recovery for the lower concentration, even using radio-labelled material. In addition, the nominal concentration of R107894 in a flow-through system can not be maintained above the required 70% recovery (i.e. in a flow-through mysid chronic study, the recovery of R107894 in the test water was only 28-43% of the nominal concentration). Two well-known and respected aquatic test laboratories that were consulted to perform the BCF study on fish, requested

Janssen to seek a solution to the technical problems with EPA before undertaking any BCF study with R107894. Running a BCF study on CL 322250 is not recommendable according to Janssen because of the low $P_{o/w}$ for this compound (1.00 at pH 7 and 0.55 at pH 8). EPA agreed to consider this issue as a priority within RASSB and respond to Janssen with technical recommendations to either perform the fish BCF study or consider waiving the study. This issue, along with the CL322248 testing (point 2) are the most pressing issues because they could dramatically and negatively affect the timeline of a June 2005 submission.

5. DE and BG discussed the timing for the Ecotox review if RASSB requires the Fish BCF study on R107894. EPA may consider a request by Janssen to proceed with the review and require the BCF study as a condition of registration based on the calculated theoretical bioconcentration factor and low $P_{o/w}$ of all the metabolites at pH 7 and 8.
6. A BCF study in oyster appears to be technically impossible because of the fast degradation in seawater and the low LC_{50} for this species. Janssen asks to reconsider this study following the outcome of the work for the BCF determination in fish, if required (see point 3 above).
7. Environmental exposure and risk assessment needs to take into account both the parent molecule R107894 and primary degradate CL 322250 using MAMPEC and/or other appropriate model. EPA risk assessors are familiar with MAMPEC. It is known that the MAMPEC model does not take degradation into account and that it is not really suitable to evaluate the degradation product (the assumption that all what leaches out of the paint is CL 322250 is an overestimate). (Janssen note – after discussing this issue with various firms with considerable experience in environmental fate and risk assessment, possibly the MAMPEC model can be used with the EXAMS model to take into account the degradation rates).
8. Janssen argued that the fish ELS study with CL 322250 should be accepted based on compliance with OECD and OPPTS 850.1400 as it has been shown that the water used was “suitable” (based on survival rates).
9. An endangered species assessment (should be included in the risk assessment considering the factors discussed in point 7. EPA recommended that Janssen to visit the ESA section on their website to learn more about the Ecological risk assessment process in OPP).
10. Janssen is requesting a waiver of the CL322250 acute avian (mallard duck) study based on the mammalian toxicity (rat) toxicity profile of the parent and metabolites. Wildlife International Ltd. provided survey data (at Janssen's request) that in only 5% of the cases is the acute rat data not a good indicator of avian toxicity.
11. EPA (JB) agreed to meet with Janssen to discuss the degradation half-lives in the various environmental fate studies (all EFATE studies were accepted by EPA) and agreed to consider Janssen's concerns in a timely manner. Janssen hopes to address these concerns in writing to EPA within 4-6 weeks.
12. EPA mentioned that EPA has some additional eco-toxicity concerns regarding stationary structures since the leachate from the paint will remain in a localized environment. EPA will check whether the additional studies that may be required to register an AF paint for use on stationary structures are already addressed by the extensive existing eco-toxicity data-base for ECONEA or advise Janssen of the additional studies required.

13. Aside from the BCF studies, all the ongoing or scheduled eco-toxicity studies should be available for submission to EPA around July 1, 2005. This would coincide with the availability of the additional ECONEA toxicity studies that Janssen has committed to submit to EPA by this same date.

Meeting Report

Subject: ECONEA Toxicology

Date: March 30, 2005

Attendees:	Dennis Edwards (DE)	EPA
	Karen Leavy-Monk (KLM)	EPA
	Tim McMahon	EPA
	Steve Malish	EPA
	Siroos Mostaghimi	EPA
	Vince Piccirillo	VJP Consulting (representing Janssen)
	Bill Goodwine (BG)	Janssen
	Piet Blancquaert	Janssen

1. The Data Evaluation Records (DERs) for the acute toxicology of ECONEA technical active ingredient have not been received. EPA (KLM) will check on the status of the review and report back to Janssen (BG); if DERs are available, copies will be provided to Janssen.
2. Janssen (BG) to provide EPA (KLM) the DERs for the acute oral and Ames mutagenicity test for R107894 (ECONEA Technical).
3. Janssen agreed to submit the following items as a single submittal on/about July 1, 2005 to allow EPA to proceed with a registration decision for the commercial/military antifouling paint:
 - a. Peer review of the neuropathology slides from the 90-day oral rat study.
 - b. 28-day dermal toxicity study in rat
 - c. Revised ECONEA Technical label with language that would restrict the use to commercial/military, as opposed to pleasure craft or stationary structures. Janssen will check with the antifouling paint manufacturers to see what is the best option.
 - d. A revised occupational risk assessment for the commercial/military use category including mixer/loader (open pour, pump liquid), and applicator (airless sprayer) using more current data. [This would include using NOEL from the 28-day dermal data for intermediate, and calculated NOEL for inhalation based on the 90-day oral study, and a percent dermal absorption calculated from the 28-day dermal and 90-day oral. Uncertainty factors are not generally applied for occupational risk assessments. EPA recommended that Janssen review some recent RED actions to see the use and usage assumptions made by EPA and consider how these relate to those used in Janssen's assessment.]
 - e. Environmental risk assessment for the military/commercial use, including an endangered species component. EPA indicated that MAMPEC is an acceptable model for this and one the Agency is familiar with.

- f. Review previously submitted use/usage information and submit revised report if necessary.
- 4. Janssen (BG) and EPA (DE) tentatively agreed on the PRIA timeline for the current ECONEA submission to be 9 months from submission of item 2 above.
- 5. Janssen will submit the following information as confirmatory for point 3(d) above and to support subsequent applications by antifoulant paint manufacturers for pleasure craft use category:
 - a. 90-day dermal rat study
 - b. 90-day inhalation rat study with FOB, motor activity and neuropathology (report will include a 14-day range-finding study)
 - c. Revised ECONEA Technical label to eliminate the language that would differentiate between commercial/military, and pleasure craft use categories.
 - d. An occupational risk assessment for the pleasure craft use category including mixer/loader (open pour), and applicator (brush/roller) using the most current data. Janssen will review some recent RED actions to assess the use and usage assumptions made by EPA in relation to those provided by the National Paint & Coatings Association (Antifouling work group).
 - e. Environmental risk assessment for the combined military/commercial and pleasure craft use patterns including a reassessment of the endangered species component. Review previously submitted use/usage information and submit revised report if necessary.
- 6. Additional general remarks:
 - a. In the 90-day oral toxicity study, brain, spinal cord and other nervous tissues were saved and histologically evaluated. The evaluation was confounded by findings in tissues from nonperfused animals that were not seen in tissues from perfused animals. For neuropathologic evaluations, perfusion provides fixed tissues that are more reliable for assessment. The EPA indicated that they would rely on the perfused animals' tissues for evaluation but the findings in nonperfused tissues raises some uncertainty. A peer review of the tissues may allay the uncertainty.
 - b. EPA was questioning whether the pleasure craft use category would include any residential (children) exposure and trigger FQPA risk assessment. Additional use and usage information for this use category, particularly the DIY segment would be useful.

DATA PACKAGE BEAN SHEET

Date: 12-Sep-2005

Page 1 of 2

Decision #: 220066

DP #: (292015)

*** Registration Information ***

Registration: 43813-ET - ECONEA TECHNICAL

Company: 43813 - JANSSEN PHARMACEUTICA INC.

Risk Manager: RM 33 - Marshall Swindell - (703) 308-6341 Room# CM-2 308H

Risk Manager Reviewer: Karen Leavy KLEAVY

Sent Date: _____ Calculated Due Date: _____ Edited Due Date: _____

Type of Registration: Product Registration - Section 3

Action Desc: _____

Ingredients: 119093, 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-(93.2%)

*** Data Package Information ***

Expedite: ☐ Yes ☒ No

Date Sent: 16-Jul-2003

Due Back: _____

DP Ingredient: 119093, 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-

DP Title: _____

CSF Included: ☒ Yes ☐ No Label Included: ☒ Yes ☐ No Parent DP #: _____

Assigned To

Date In

Date Out

Organization: AD / RASSB

23-Apr-2004

Last Possible Science Due Date: 24-Dec-2006

Team Name: RASSB3

01-Aug-2003

19-Apr-2004

Science Due Date: _____

Reviewer Name: Petrie, Richard

01-Aug-2003

19-Apr-2004

Sub Data Package Due Date: _____

Contractor Name: _____

*** Studies Sent for Review ***

No Studies

*** Additional Data Package for this Decision ***

Printed on Page 2

*** Data Package Instructions ***

Please review the following ecotoxicity studies for acceptability-(MRID Nos. 45893901, 45893902, 45893903, 45893904, 45893905, 45945201, 45893906, 45893907, and 45893908). Data submitted in response to Agency's letter of March, 2003.

DATA PACKAGE BEAN SHEET

Date: 08-Sep-2005

Page 1 of 2

***** Registration Information *****Registration: 43813-ET - ECONEA TECHNICALCompany: 43813 - JANSSEN PHARMACEUTICA INC.Risk Manager: RM 33 - Marshall Swindell - (703) 308-6341 Room# CM-2 308HRisk Manager Reviewer: Karen Leavy KLEAVYSent Date: 12-May-2005Calculated Due Date: 08-Jan-2007

Edited Due Date: _____

Type of Registration: Product Registration - Section 3Action Desc: (A41) NEW AI;NON-FOOD USE;OUTDOOR;OTHER USES;Ingredients: 119093, 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-(93.2%)***** Data Package Information *****Expedite: ☐ Yes ☒ NoDate Sent: 08-Sep-2005

Due Back: _____

DP Ingredient: 119093, 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-DP Title: Ecological Effects StudiesCSF Included: ☒ Yes ☐ NoLabel Included: ☒ Yes ☐ No

Parent DP #: _____

Assigned To**Date In****Date Out**Organization: AD / RASSBLast Possible Science Due Date: 03-Jul-2006Team Name: RASSB1

Science Due Date: _____

Reviewer Name: _____

Sub Data Package Due Date: _____

Contractor Name: _____

***** Studies Sent for Review *****

No Studies

***** Additional Data Package for this Decision *****

Printed on Page 2

***** Data Package Instructions *****

Please review the following Ecological Effects studies(Rick). MRID#S 456960-06, -14, and 466199-01.

Receipt for Section 3

S: 782775

Resubmission: ☒ Yes ☐ No

Regulatory Type: Product Registration - Section 3

Fee For Service: ☒ Yes ☐ No

Application Type: New Registration

Billable: ☐ Yes ☒ No

Company: 43813 JANSSEN PHARMACEUTICA INC.



Print Letter

Enter More Information

Tracking

Risk Manager: Antimicrobials Division, Risk Management Team 33

Product #: 43813-ET

Product Name: ECONEA TECHNICAL

Override#

Me Too

Section3:

Me Too

Product Name:

Application Date: 10-Aug-2005



OPP Rec'd Date: 10-Aug-2005



Front End Date: 10-Aug-2005



Risk Manager Send Date: 10-Aug-2005



FFS Due Date:

Negotiated Due Date:

OPP Target Date:

Receipt Content

Study

Fast Track: ☐

New Ingredient: ☐

Receipt Description:

resubmission following 86-5 rejection

New Ingredient

Request Date:

New Ingredient

Received Date:

Form A: ☐

Signature Date:

Form B: ☐

Signature Date:

JANSSEN



PHARMACEUTICA INC.

466199-00

July 14, 2005

Document Processing Desk 7504C)
U.S. Environmental Protection Agency
Office of Pesticide Programs
Antimicrobial Division (7510W)
Regulatory Management Branch II
1801 South Bell Street
Arlington, VA 22202-4501

RE: ECONEAT™ Technical – Janssen Code# R107894 (EPA File 43813-ET)
Supplemental Submission for 158 Subpart D Wildlife & Aquatic Organisms
EPA Letter of June 1, 2004

Attn.: Mr. Marshall Swindell
Product Manager/Team 33

Referring to EPA deficiency letter dated June 1, 2004, Janssen Pharmaceutica Inc. is providing the following additional ecotoxicology studies (in triplicate):

ECO-TOXICITY (40 CFR 158.490)

Parent Compound R107894.

Volume 1 R107894 - Acute toxicity to Water Fleas, (*Daphnia magna*) Under Flow-Through Conditions, Springborn-Smithers Laboratories, Report No. 13751.6144 (Janssen Rpt. No. AGR 921), June 28, 2005, OPPTS Draft Guideline 850.1010

MRID

46596001

Volume 2 R107894 - Acute Toxicity to Rainbow Trout (*Oncorhynchus mykiss*) Under Flow-Through Conditions, Springborn Smithers Laboratories, Report No. 13751.6143, (Janssen Rpt. No. AGR 920), April 29, 2005, OPPTS Draft Guideline 850.1075.

MRID

46596002



Volume 3 R107894 – Acute Toxicity to Bluegill Sunfish (*Lepomis macrochirus*) Under Flow-Through Conditions, Springborn Smithers Laboratories, Report No. 13751.6142, (Janssen Rpt. No. AGR 919), April 11, 2005, OPPTS Draft Guideline No. 850.1075

MRID 46596003

Volume 4 R107894- Full Life-Cycle Toxicity Test with Water Fleas, *Daphnia magna* Under Flow-Through Conditions, Springborn Smithers Laboratories, Report No. 13751.6145, (Janssen Rpt. No. AGR 922), June 27, 2005, OPPTS Draft Guideline 850.1300

MRID 46596004

Volume 5 R107894- A Dietary LC50 Study with The Mallard, Report No. 168-101B, (Janssen Rpt. No. AGR 916), July 8, 2005, Wildlife International, Ltd., OPPTS Draft Guideline 850.2200

MRID 46596005

PLANT PROTECTION/NONTARGET PLANTS (40 CFR 158.540)

Parent Compound R107894

Volume 6 R107894- Acute Toxicity to the Freshwater Green Alga, *Pseudokirchneriella subcapitata*, Springborn Smithers Laboratories, Report No. 13751.6146 (Janssen Rpt. No. AGR 1025), March 17, 2005, OPPTS Draft Guideline 850.5400.

MRID 46596006



Volume 7 R107894 – Acute Toxicity to the Marine Diatom, *Skeletonema costatum*, Under Static Conditions, Springborn Smithers Laboratories,
Report No. 13751.6147, (Janssen Rpt. No. AGR 1026), March 17, 2005,
OPPTS Draft Guideline 850.5400

MRID

46619901**ECO-TOXICITY (40 CFR 158.490)*****Metabolite CL 322,250***

Volume 8 CL 322,250 – Acute Toxicity to Water Fleas, (*Daphnia magna*)
Under Flow-Through Conditions, Springborn Smithers Laboratories,
Report No. 13751.6151 (Janssen Rpt. No. AGR 925), June 28, 2005, OPPTS Draft Guideline 850.1010

MRID

46596008

Volume 9 CL 322,250 – Acute Toxicity to Bluegill Sunfish (*Lepomis macrochirus*), Under Flow-Through Conditions, Springborn Smithers Laboratories, Report No. 13751.6149 (Janssen Rpt. No. AGR923), May 9, 2005, OPPTS Draft Guideline 850.1075

MRID

46596009

Volume 10 CL 322,250 – Acute Toxicity to Rainbow Trout (*Oncorhynchus mykiss*), Under Flow-Through Conditions, Springborn Smithers Laboratories, Report No. 13751/6150 (Janssen Rpt. No. 924), April 26, 2005,
OPPTS Draft Guideline 850.1075.

MRID

46596010



Volume 11 CL 322,250 – Full Life-Cycle Toxicity Test with Water Fleas (*Daphnia magna*) Under Flow-Through Conditions, Springborn Smithers Laboratories, Report No. 13751.6152 (Janssen Rpt. No. AGR 926), June 27, 2005, OPPTS Draft Guideline 850.1300

MRID 46596011

Volume 12 CL 322,250 – Life-Cycle Toxicity Test with Mysids (*Americamysis bahia*), Springborn Smithers Laboratories, Report No. 13751-6153 (Janssen Rpt. No. AGR 927), July 11, 2005, OPPTS Draft Guideline 850.1350

MRID 46596012

Volume 13 CL 322,250 – A Dietary LC50 Study with the Mallard, Report No. 168-102 (Janssen Rpt. No. AGR 1116), July 8, 2005, Wildlife International, Ltd., OPPTS Draft Guideline 850.2200

MRID 46596013

PLANT PROTECTION/NONTARGET PLANTS (40 CFR 158.540)

Metabolite CL 322,250

Volume 14 CL 322,250 – Acute Toxicity to the Marine Diatom, *Skeletonema costatum*, Under Static Conditions, Springborn Smithers Laboratories, Report No. 13751.6154, (Janssen Rpt. No. AGR 1027), April 15, 2005, OPPTS Draft Guideline 850.5400

MRID 46596014

JANSSEN



PHARMACEUTICA INC.

Please contact me directly on any matters relating to this submission. I can be reached by phone at 609-730-2607.

Sincerely,

Bill Goodwin

William R. Goodwin
Senior Director
Regulatory Affairs & Product development
Plant & Material Protection Division
Tel: 609/730-2607
Fax: 609/730-2411
Email: bgoodwin@janus.jnj.com

MEMORANDUM

DATE: 8/11/05

TO: AD (33), Regulatory Manager

FROM: Information Services Branch, IRSD

Your receipt of this data submission is not an indication that MRIDs for the enclosed studies have been posted in OPPIN.

We expect that it will be approximately 5 days from the above date before the study-level data is available in OPPIN.

If you have any questions about this process, please contact Maureen Sherrill (305-5361) or Teresa Downs (305-5363).

This is a: ☒ fully accepted submission
☐ partially accepted submission
☐ rejected submission



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

August 10, 2005

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

JANSSEN PHARMACEUTICA INC.
PLANT PROTECTION DIVISION
1125 TRENTON-HARBOURTON RD
TITUSVILLE, NJ 08560-0200

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your submittal of 10-AUG-05. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your submittal was found to be in full compliance with the standards for submission of data contained in PR Notice 86-5. A copy of your bibliography is enclosed, annotated with Master Record ID's (MRIDs) assigned to each document submitted. Please use these numbers in all future references to these documents. Thank you for your cooperation. If you have any questions concerning this data submission, please raise them with the cognizant Product Manager, to whom the data have been released.

JANSSEN**PHARMACEUTICA INC.**

466199-00

July 14, 2005

Document Processing Desk 7504C)
U.S. Environmental Protection Agency
Office of Pesticide Programs
Antimicrobial Division (7510W)
Regulatory Management Branch II
1801 South Bell Street
Arlington, VA 22202-4501

RE: ECONEA™ Technical – Janssen Code# R107894 (EPA File 43813-ET)
Supplemental Submission for 158 Subpart D Wildlife & Aquatic Organisms
EPA Letter of June 1, 2004

Attn.: Mr. Marshall Swindell
Product Manager/Team 33

Referring to EPA deficiency letter dated June 1, 2004, Janssen Pharmaceutica Inc. is providing the following additional ecotoxicology studies (in triplicate):

ECO-TOXICITY (40 CFR 158.490)***Parent Compound R107894.***

Volume 1 R107894 - Acute toxicity to Water Fleas, (*Daphnia magna*) Under Flow-Through Conditions, Springborn-Smithers Laboratories, Report No. 13751.6144 (Janssen Rpt. No. AGR 921), June 28, 2005, OPPTS Draft Guideline 850.1010

MRID

46596001

Volume 2 R107894 - Acute Toxicity to Rainbow Trout (*Oncorhynchus mykiss*) Under Flow-Through Conditions, Springborn Smithers Laboratories, Report No. 13751.6143, (Janssen Rpt. No. AGR 920), April 29, 2005, OPPTS Draft Guideline 850.1075.

MRID

46596002



Volume 3 R107894 – Acute Toxicity to Bluegill Sunfish (*Lepomis macrochirus*) Under Flow-Through Conditions, Springborn Smithers Laboratories, Report No. 13751.6142, (Janssen Rpt. No. AGR 919), April 11, 2005, OPPTS Draft Guideline No. 850.1075

MRID 46596003

Volume 4 R107894- Full Life-Cycle Toxicity Test with Water Fleas, *Daphnia magna* Under Flow-Through Conditions, Springborn Smithers Laboratories, Report No. 13751.6145, (Janssen Rpt. No. AGR 922), June 27, 2005, OPPTS Draft Guideline 850.1300

MRID 46596004

Volume 5 R107894- A Dietary LC50 Study with The Mallard, Report No. 168-101B, (Janssen Rpt. No. AGR 916), July 8, 2005, Wildlife International, Ltd., OPPTS Draft Guideline 850.2200

MRID 46596005

PLANT PROTECTION/NONTARGET PLANTS (40 CFR 158.540)

Parent Compound R107894

Volume 6 R107894- Acute Toxicity to the Freshwater Green Alga, *Pseudokirchneriella subcapitata*, Springborn Smithers Laboratories, Report No. 13751.6146 (Janssen Rpt. No. AGR 1025), March 17, 2005, OPPTS Draft Guideline 850.5400.

MRID 46596006



Volume 7 R107894 – Acute Toxicity to the Marine Diatom, *Skeletonema costatum*, Under Static Conditions, Springborn Smithers Laboratories,
Report No. 13751.6147, (Janssen Rpt. No. AGR 1026), March 17, 2005,
OPPTS Draft Guideline 850.5400

MRID

46619901**ECO-TOXICITY (40 CFR 158.490)*****Metabolite CL 322,250***

Volume 8 CL 322,250 – Acute Toxicity to Water Fleas, (*Daphnia magna*)
Under Flow-Through Conditions, Springborn Smithers Laboratories,
Report No. 13751.6151 (Janssen Rpt. No. AGR 925), June 28, 2005, OPPTS Draft Guideline 850.1010

MRID

46596008

Volume 9 CL 322,250 – Acute Toxicity to Bluegill Sunfish (*Lepomis macrochirus*), Under Flow-Through Conditions, Springborn Smithers Laboratories, Report No. 13751.6149 (Janssen Rpt. No. AGR923), May 9, 2005, OPPTS Draft Guideline 850.1075

MRID

46596009

Volume 10 CL 322,250 – Acute Toxicity to Rainbow Trout (*Oncorhynchus mykiss*), Under Flow-Through Conditions, Springborn Smithers Laboratories, Report No. 13751/6150 (Janssen Rpt. No. 924), April 26, 2005,
OPPTS Draft Guideline 850.1075.

MRID

46596010



Volume 11 CL 322,250 – Full Life-Cycle Toxicity Test with Water Fleas (*Daphnia magna*) Under Flow-Through Conditions, Springborn Smithers Laboratories, Report No. 13751.6152 (Janssen Rpt. No. AGR 926), June 27, 2005, OPPTS Draft Guideline 850.1300

MRID 46596011

Volume 12 CL 322,250 – Life-Cycle Toxicity Test with Mysids (*Americamysis bahia*), Springborn Smithers Laboratories, Report No. 13751-6153 (Janssen Rpt. No. AGR 927), July 11, 2005, OPPTS Draft Guideline 850.1350

MRID 46596012

Volume 13 CL 322,250 – A Dietary LC50 Study with the Mallard, Report No. 168-102 (Janssen Rpt. No. AGR 1116), July 8, 2005, Wildlife International, Ltd., OPPTS Draft Guideline 850.2200

MRID 46596013

PLANT PROTECTION/NONTARGET PLANTS (40 CFR 158.540)

Metabolite CL 322,250

Volume 14 CL 322,250 – Acute Toxicity to the Marine Diatom, *Skeletonema costatum*, Under Static Conditions, Springborn Smithers Laboratories, Report No. 13751.6154, (Janssen Rpt. No. AGR 1027), April 15, 2005, OPPTS Draft Guideline 850.5400

MRID 46596014

JANSSEN



PHARMACEUTICA INC.

Please contact me directly on any matters relating to this submission. I can be reached by phone at 609-730-2607.

Sincerely,

Bill Goodwine

William R. Goodwine
Senior Director
Regulatory Affairs & Product development
Plant & Material Protection Division
Tel: 609/730-2607
Fax: 609/730-2411
Email: bgoodwin@janus.jnj.com

Administrative

Materials

JANSSEN**PHARMACEUTICA INC.****FACSIMILE TRANSMITTAL**

Date: August 1, 2005

To: Ms. Karen Leavy
U.S. EPA

Fax: 703/308-6467

From: Joanne Haman-Hoy on behalf of
Bill Goodwine
Janssen Pharmaceutica Inc.Phone: 609/730-2607 (B. Goodwine)
609/730-2609 (J. Haman-Hoy)

Fax: 609/730-3138

Pages: 2 Including Cover

Re: ECONEA™ Technical Submission

Dear Ms. Leavy:

As per our phone conversation this afternoon, attached is the missing page 44 from ***Volume 7** of 14 for Janssen's ECONEA™ Technical supplemental submission for 158 subpart D Wildlife & Aquatic Organisms [EPA's letter of June 1, 2004].

***Volume 7:** R107894 - Acute Toxicity to the Marine Diatom, *Skeletonema costatum*, Under Static Conditions, Springborn Smithers Laboratories, Report No. 13751.6147 (Janssen Report No. AGR 1026), March 17, 2005. OPPTS Draft Guideline 850.5400.

I can be reached at 609/730-2609 if you require any additional information.

Best Regards,

Joanne Haman-Hoy



1125 TRENTON-HARBOURTON ROAD
POST OFFICE BOX 200
TITUSVILLE, NEW JERSEY 08560-0200
(609) 730-2000

us.janssen.com

Data was rejected
because page 44
was missing. Page 44
has been inserted.
Now, the data needs
MR ID No.
K. Leavy



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

July 21, 2005

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

JANSSEN PHARMACEUTICA INC.
1125 TRENTON-HARBOURTON RD
TITUSVILLE, NJ 08560-0200

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your submittal of 18-JUL-05. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your data submittal was found to be partially in compliance with the standards for submission of data contained in PR Notice 86-5, with the exceptions noted below. A copy of your transmittal bibliography is enclosed, annotated with the Master Record ID's (MRIDs) assigned to each document accepted. Please use these numbers in all future references to these documents.

If deficiencies were found which apply to individual accepted studies, they are listed below following the applicable MRID. Any document which has been assigned a MRID has been accepted under PR Notice 86-5. If any comments related to a MRID appear on this report, they are provided for your information and reference when preparing future submissions. Some individual documents were not acceptable, and all copies are being returned to you for correction for the reasons indicated below.

These rejected studies have been assigned separate identification numbers which are annotated on both the enclosed bibliography and the rejected document labels.

The rejected studies and their deficiencies are described below.

Rejected Study [07]:

* Judging from the pagination of the study, pages 44 were omitted from the submitted copy.



July 14, 2005

Document Processing Desk 7504C)
U.S. Environmental Protection Agency
Office of Pesticide Programs
Antimicrobial Division (7510W)
Regulatory Management Branch II
1801 South Bell Street
Arlington, VA 22202-4501

RE: ECONEAT™ Technical – Janssen Code# R107894 (EPA File 43813-ET)
Supplemental Submission for 158 Subpart D Wildlife & Aquatic Organisms
EPA Letter of June 1, 2004

Attn.: Mr. Marshall Swindell
Product Manager/Team 33

Referring to EPA deficiency letter dated June 1, 2004, Janssen Pharmaceutica Inc. is providing the following additional ecotoxicology studies (in triplicate):

ECO-TOXICITY (40 CFR 158.490)

Parent Compound R107894

Volume 1 R107894 - Acute toxicity to Water Fleas, (*Daphnia magna*) Under Flow-Through Conditions, Springborn-Smithers Laboratories, Report No. 13751.6144 (Janssen Rpt. No. AGR 921), June 28, 2005, OPPTS Draft Guideline 850.1010

MRID

46596001

Volume 2 R107894 - Acute Toxicity to Rainbow Trout (*Oncorhynchus mykiss*) Under Flow-Through Conditions, Springborn Smithers Laboratories, Report No. 13751.6143, (Janssen Rpt. No. AGR 920), April 29, 2005, OPPTS Draft Guideline 850.1075.

MRID

46596002



Volume 3 R107894 – Acute Toxicity to Bluegill Sunfish (*Lepomis macrochirus*) Under Flow-Through Conditions, Springborn Smithers Laboratories, Report No. 13751.6142, (Janssen Rpt. No. AGR 919), April 11, 2005, OPPTS Draft Guideline No. 850.1075

MRID 46596003

Volume 4 R107894- Full Life-Cycle Toxicity Test with Water Fleas, *Daphnia magna* Under Flow-Through Conditions, Springborn Smithers Laboratories, Report No. 13751.6145, (Janssen Rpt. No. AGR 922), June 27, 2005, OPPTS Draft Guideline 850.1300

MRID 46596004

Volume 5 R107894- A Dietary LC50 Study with The Mallard, Report No. 168-101B, (Janssen Rpt. No. AGR 916), July 8, 2005, Wildlife International, Ltd., OPPTS Draft Guideline 850.2200

MRID 46596005

PLANT PROTECTION/NONTARGET PLANTS (40 CFR 158.540)

Parent Compound R107894

Volume 6 R107894- Acute Toxicity to the Freshwater Green Alga, *Pseudokirchneriella subcapitata*, Springborn Smithers Laboratories, Report No. 13751.6146 (Janssen Rpt. No. AGR 1025), March 17, 2005, OPPTS Draft Guideline 850.5400.

MRID 46596006



Volume 7 R107894 – Acute Toxicity to the Marine Diatom, *Skeletonema costatum*, Under Static Conditions, Springborn Smithers Laboratories,
Report No. 13751.6147, (Janssen Rpt. No. AGR 1026), March 17, 2005,
OPPTS Draft Guideline 850.5400

MRID

Reject (07)

ECO-TOXICITY (40 CFR 158.490)***Metabolite CL 322,250***

Volume 8 CL 322,250 – Acute Toxicity to Water Fleas, (*Daphnia magna*) Under Flow-Through Conditions, Springborn Smithers Laboratories,
Report No. 13751.6151 (Janssen Rpt. No. AGR 925), June 28, 2005, OPPTS Draft Guideline 850.1010

MRID

46596008

Volume 9 CL 322,250 – Acute Toxicity to Bluegill Sunfish (*Lepomis macrochirus*), Under Flow-Through Conditions, Springborn Smithers Laboratories, Report No. 13751.6149 (Janssen Rpt. No. AGR923), May 9, 2005, OPPTS Draft Guideline 850.1075

MRID

46596009

Volume 10 CL 322,250 – Acute Toxicity to Rainbow Trout (*Oncorhynchus mykiss*), Under Flow-Through Conditions, Springborn Smithers Laboratories, Report No. 13751/6150 (Janssen Rpt. No. 924), April 26, 2005,
OPPTS Draft Guideline 850.1075.

MRID

46596010



Volume 11 CL 322,250 – Full Life-Cycle Toxicity Test with Water Fleas (*Daphnia magna*) Under Flow-Through Conditions, Springborn Smithers Laboratories, Report No. 13751.6152 (Janssen Rpt. No. AGR 926), June 27, 2005, OPPTS Draft Guideline 850.1300

MRID 46596011

Volume 12 CL 322,250 – Life-Cycle Toxicity Test with Mysids (*Americamysis bahia*), Springborn Smithers Laboratories, Report No. 13751-6153 (Janssen Rpt. No. AGR 927), July 11, 2005, OPPTS Draft Guideline 850.1350

MRID 46596012

Volume 13 CL 322,250 – A Dietary LC50 Study with the Mallard, Report No. 168-102 (Janssen Rpt. No. AGR 1116), July 8, 2005, Wildlife International, Ltd., OPPTS Draft Guideline 850.2200

MRID 46596013

PLANT PROTECTION/NONTARGET PLANTS (40 CFR 158.540)

Metabolite CL 322,250

Volume 14 CL 322,250 – Acute Toxicity to the Marine Diatom, *Skeletonema costatum*, Under Static Conditions, Springborn Smithers Laboratories, Report No. 13751.6154, (Janssen Rpt. No. AGR 1027), April 15, 2005, OPPTS Draft Guideline 850.5400

MRID 46596014

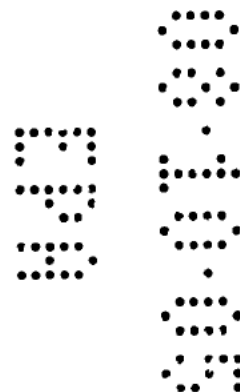


Please contact me directly on any matters relating to this submission. I can be reached by phone at 609-730-2607.

Sincerely,

Bill Goodwine

William R. Goodwine
Senior Director
Regulatory Affairs & Product development
Plant & Material Protection Division
Tel: 609/730-2607
Fax: 609/730-2411
Email: bgoodwin@janus.jnj.com





UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

July 21, 2005

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

JANSSEN PHARMACEUTICA INC.
1125 TRENTON-HARBOURTON RD
TITUSVILLE, NJ 08560-0200

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your submittal of 18-JUL-05. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your data submittal was found to be partially in compliance with the standards for submission of data contained in PR Notice 86-5, with the exceptions noted below. A copy of your transmittal bibliography is enclosed, annotated with the Master Record ID's (MRIDs) assigned to each document accepted. Please use these numbers in all future references to these documents.

If deficiencies were found which apply to individual accepted studies, they are listed below following the applicable MRID. Any document which has been assigned a MRID has been accepted under PR Notice 86-5. If any comments related to a MRID appear on this report, they are provided for your information and reference when preparing future submissions. Some individual documents were not acceptable, and all copies are being returned to you for correction for the reasons indicated below.

These rejected studies have been assigned separate identification numbers which are annotated on both the enclosed bibliography and the rejected document labels.

The rejected studies and their deficiencies are described below.

Rejected Study [07]:

* Judging from the pagination of the study, pages 44 were omitted from the submitted copy.



July 14, 2005

Document Processing Desk 7504C)
U.S. Environmental Protection Agency
Office of Pesticide Programs
Antimicrobial Division (7510W)
Regulatory Management Branch II
1801 South Bell Street
Arlington, VA 22202-4501

RE: ECONEAT™ Technical – Janssen Code# R107894 (EPA File 43813-ET)
Supplemental Submission for 158 Subpart D Wildlife & Aquatic Organisms
EPA Letter of June 1, 2004

Attn.: Mr. Marshall Swindell
Product Manager/Team 33

Referring to EPA deficiency letter dated June 1, 2004, Janssen Pharmaceutica Inc. is providing the following additional ecotoxicology studies (in triplicate):

ECO-TOXICITY (40 CFR 158.490)

Parent Compound R107894

Volume 1 R107894 - Acute toxicity to Water Fleas, (*Daphnia magna*) Under Flow-Through Conditions, Springborn-Smithers Laboratories, Report No. 13751.6144 (Janssen Rpt. No. AGR 921), June 28, 2005, OPPTS Draft Guideline 850.1010

MRID

46596001

Volume 2 R107894 - Acute Toxicity to Rainbow Trout (*Oncorhynchus mykiss*) Under Flow-Through Conditions, Springborn Smithers Laboratories, Report No. 13751.6143, (Janssen Rpt. No. AGR 920), April 29, 2005, OPPTS Draft Guideline 850.1075.

MRID

46596002



Volume 3 R107894 – Acute Toxicity to Bluegill Sunfish (*Lepomis macrochirus*) Under Flow-Through Conditions, Springborn Smithers Laboratories, Report No. 13751.6142, (Janssen Rpt. No. AGR 919), April 11, 2005, OPPTS Draft Guideline No. 850.1075

MRID 46596003

Volume 4 R107894- Full Life-Cycle Toxicity Test with Water Fleas, *Daphnia magna* Under Flow-Through Conditions, Springborn Smithers Laboratories, Report No. 13751.6145, (Janssen Rpt. No. AGR 922), June 27, 2005, OPPTS Draft Guideline 850.1300

MRID 46596004

Volume 5 R107894- A Dietary LC50 Study with The Mallard, Report No. 168-101B, (Janssen Rpt. No. AGR 916), July 8, 2005, Wildlife International, Ltd., OPPTS Draft Guideline 850.2200

MRID 46596005

PLANT PROTECTION/NONTARGET PLANTS (40 CFR 158.540)

Parent Compound R107894

Volume 6 R107894- Acute Toxicity to the Freshwater Green Alga, *Pseudokirchneriella subcapitata*, Springborn Smithers Laboratories, Report No. 13751.6146 (Janssen Rpt. No. AGR 1025), March 17, 2005, OPPTS Draft Guideline 850.5400.

MRID 46596006



Volume 7 R107894 – Acute Toxicity to the Marine Diatom, *Skeletonema costatum*, Under Static Conditions, Springborn Smithers Laboratories,
Report No. 13751.6147, (Janssen Rpt. No. AGR 1026), March 17, 2005,
OPPTS Draft Guideline 850.5400

MRID

Reject (07)

ECO-TOXICITY (40 CFR 158.490)***Metabolite CL 322,250***

Volume 8 CL 322,250 – Acute Toxicity to Water Fleas, (*Daphnia magna*) Under Flow-Through Conditions, Springborn Smithers Laboratories,
Report No. 13751.6151 (Janssen Rpt. No. AGR 925), June 28, 2005, OPPTS Draft Guideline 850.1010

MRID

46596008

Volume 9 CL 322,250 – Acute Toxicity to Bluegill Sunfish (*Lepomis macrochirus*), Under Flow-Through Conditions, Springborn Smithers Laboratories, Report No. 13751.6149 (Janssen Rpt. No. AGR923), May 9, 2005, OPPTS Draft Guideline 850.1075

MRID

46596009

Volume 10 CL 322,250 – Acute Toxicity to Rainbow Trout (*Oncorhynchus mykiss*), Under Flow-Through Conditions, Springborn Smithers Laboratories, Report No. 13751/6150 (Janssen Rpt. No. 924), April 26, 2005,
OPPTS Draft Guideline 850.1075.

MRID

46596010



Volume 11 CL 322,250 – Full Life-Cycle Toxicity Test with Water Fleas (*Daphnia magna*) Under Flow-Through Conditions, Springborn Smithers Laboratories, Report No. 13751.6152 (Janssen Rpt. No. AGR 926), June 27, 2005, OPPTS Draft Guideline 850.1300

MRID 46596011

Volume 12 CL 322,250 – Life-Cycle Toxicity Test with Mysids (*Americamysis bahia*), Springborn Smithers Laboratories, Report No. 13751-6153 (Janssen Rpt. No. AGR 927), July 11, 2005, OPPTS Draft Guideline 850.1350

MRID 46596012

Volume 13 CL 322,250 – A Dietary LC50 Study with the Mallard, Report No. 168-102 (Janssen Rpt. No. AGR 1116), July 8, 2005, Wildlife International, Ltd., OPPTS Draft Guideline 850.2200

MRID 46596013

PLANT PROTECTION/NONTARGET PLANTS (40 CFR 158.540)

Metabolite CL 322,250

Volume 14 CL 322,250 – Acute Toxicity to the Marine Diatom, *Skeletonema costatum*, Under Static Conditions, Springborn Smithers Laboratories, Report No. 13751.6154, (Janssen Rpt. No. AGR 1027), April 15, 2005, OPPTS Draft Guideline 850.5400

MRID 46596014

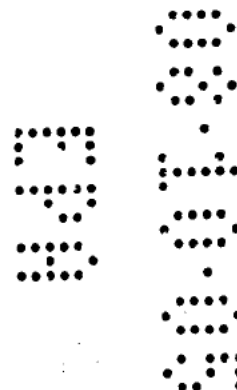


Please contact me directly on any matters relating to this submission. I can be reached by phone at 609-730-2607.

Sincerely,

Bill Goodwine

William R. Goodwine
Senior Director
Regulatory Affairs & Product development
Plant & Material Protection Division
Tel: 609/730-2607
Fax: 609/730-2411
Email: bgoodwin@janus.jnj.com



ECONEA® 028

Technical

Anti-fouling Preservative

For Formulating Use Only

ACTIVE INGREDIENT:

Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl)

93.2%

INERT INGREDIENTS:

6.8%

TOTAL:

100.0%

KEEP OUT OF REACH OF CHILDREN



DANGER

POISON

See side panel for first aid and additional precautionary statements

EPA Reg. No.: 43813-xx

EPA Est. No.: 241-MO-001

JANSSEN PHARMACEUTICA

1125 Trenton-Harbourton Road

Titusville, NJ 08560

Rev. 01/04

PRECAUTIONARY STATEMENT
HAZARDS TO HUMANS AND DOMESTIC ANIMALS
DANGER

Fatal if swallowed. Harmful if inhaled or absorbed through the skin. Causes moderate eye irritation. Avoid breathing dust. Avoid contact with skin, eyes, or clothing. Wash hands thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco. Remove contaminated clothing and wash clothing before reuse.

Handler Personal Protective Equipment (PPE):

- Wear long-sleeved shirt, long pants, socks, shoes, and chemical resistant natural rubber gloves.
- Wear protective eyewear such as goggles, face shield or safety glasses.
- Wear dust filtering respirator (MSHA/NIOSH approval number prefix TC-21C), or a NIOSH approved respirator with any N, R, P, or HE filter.

Pesticide User Safety Requirements:

Discard clothing and other absorbent materials that have been heavily contaminated with this product. Do not reuse them. Follow the manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry.

FIRST AID	
If swallowed	-Call a poison control center or doctor immediately for treatment advice. -Have person sip a glass of water if able to swallow. -Do not induce vomiting unless told to do so by a poison control center or doctor. -Do not give anything by mouth to an unconscious person.
If inhaled	-Move person to fresh air. -If person is not breathing, call 911 or an ambulance, then give artificial respiration, preferably mouth-to-mouth if possible. -Call a poison control center or doctor for further treatment advice
If in eyes	-Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing eye. -Call a poison control center or doctor for treatment advice.
If on skin or clothing	-Take off contaminated clothing. -Rinse skin immediately with plenty of water for 15-20 minutes. -Call a poison control center or doctor for treatment advice.
HOT LINE NUMBER: Chem Trec: (800) 424-9300 Have the product container with you when calling a poison control center or doctor, or going for treatment.	
NOTE TO PHYSICIAN Probable mucosal damage may contraindicate the use of gastric lavage.	

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

This product is intended for use only during industrial formulation processes producing antifouling products for control of hard fouling organisms. For use in antifouling paints, the active ingredient in ECONEA 028 should be incorporated at up to 6% of the total weight of the final paint formulation. Formulators using ECONEA 028 are responsible for providing additional data to support registration of their end-use product(s).

STORAGE AND DISPOSAL

PROHIBITIONS: Do not contaminate water, food or feed by storage and disposal.

STORAGE: DO NOT mix or store this product or solutions of this product in a manner inconsistent with its labeling.

DISPOSAL: Pesticide wastes may be acutely hazardous. Improper disposal is a violation of Federal Law.

PESTICIDE DISPOSAL: Pesticide, mixtures, or equipment rinse waters that cannot be chemically reprocessed must be disposed of according to applicable federal, state or local procedures. Contact your State Pesticide or Environmental Control Agency or the Hazardous Waste representative at the nearest EPA Regional Office for guidance.

CONTAINER DISPOSAL: Completely empty liner by shaking and tapping sides and bottom to loosen clinging particles. Empty residue into formulation equipment. Then dispose of liner in a sanitary landfill or by incineration if allowed by State and local authorities. If burned, stay out of smoke. If drum is contaminated and cannot be reused, dispose of in the same manner.

ENVIRONMENTAL HAZARDS

Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA.

NOTICE OF WARRANTY

Janssen Pharmaceutica warrants that this product conforms to the chemical description on the label thereof and is reasonably fit for purposes stated on such label only when used in accordance with the directions under normal use conditions. It is impossible to eliminate all risks inherently associated with the use of this product. Ineffectiveness or other unintended consequences may result because of such factors as weather conditions, presence of other materials, or the manner of use or application, all of which are beyond the control of Janssen Pharmaceutica. In no case shall Janssen Pharmaceutica be liable for consequential, special or indirect damages resulting from the use or handling of this product. The Buyer shall assume all such risks. **Janssen Pharmaceutica makes no warranties of merchantability of fitness for a particular purpose or any other express or implied warranty except as stated above.**

SUBMISSION BAR CODE #

778408

REVIEWER

RD

Decision #

220066

01-08-07

CODING FORM FOR APPLICATIONS FOR REGISTRATION/AMENDMENTS

FILE SYMBOL/REG NO. 43813-ET PM 33 ACTION CODE A41

DESCRIPTOR

☐ CHILD RESISTANT PACKAGING: ☐ CERTIFICATION
☐ NON-RESIDENTIAL USE ONLY
☐ NOT APPLICABLE

REGISTRATION TYPE: ☐ CONDITIONAL ☐ UNCONDITIONALPROPOSED CLASSIFICATION: ☐ GENERAL ☐ RESTRICTED USE

DATE ON APPLICATION

EPA RECEIVE DATE

PM RECEIVE DATE

05 02 05

05 04 05

05 04 05

METHOD OF SUPPORT

FORMULATORS EXEMPTION

☐ CITE ALL
☐ SELECTIVE
☐ NOT SUBMITTED
☐ NOT APPLICABLE
☐ INCORRECT/RESUB

☐ SUBMITTED
☐ NOT SUBMITTED
☐ NOT APPLICABLE
☐ INCORRECT/RESUB

REVIEW(S) REQUESTED

DATA
PACK #DATE
SENTDUE
DATEDATE
RETURNED

CHEMISTRY

EFFICACY

TOXICOLOGY

HED TOX.

ENVIRON. FATE

FISH/WILDLIFE

OTHER

STATUS

RESPONSE CODE

//

RESPONSE DATE

JUL 12 2005

39



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

JUL 12 2005

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Mr. William Goodwine
Senior Director of the Plant & Material Protection Division for,
Janssen Pharmaceutica, Inc.
11215 Trenton-Harbourton Road
Titusville, NJ 08560

Subject: ECONEA TM Technical
EPA File Symbol 43813-ET
Your Submission Dated January 17th, 2005
EPA Received Date January 24th, 2005

The submission referred to above, submitted in connection with registration under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, in response to our letter of June 1st, 2004, concerning the ecological effects review, is unacceptable.

The Agency's findings are as follows:

Bioconcentration Factor Waiver Request:

Based on these results, the Agency agrees that no further bioconcentration testing is required for ECONEA or its major metabolites, and recommends that the waiver request for bioconcentration testing in fish(165-4/180.1730) and oyster(165-4/850.1710) be granted.

Avian Dietary Waiver Request:

A single avian dietary test on CL 322248 using the mallard will provide concrete evidence of the comparative toxicity of CL 322248 vs CL3222350 and R107894. Data on all of these compounds will be of value in conducting a risk assessment for regulatory decision-making. Therefore, the waiver request for an avian dietary study on CL322248 will not be granted.

Request to Upgrade Sheepshead Minnow Acute Study to be Acceptable(MRID No. 456741-01):

Since the acute Sheepshead minnow testing with CL322250 metabolite is substantially less toxic than the parent ECONEA (R107894), the CL322250 marine/estuarine fish study does not need to be repeated. However, the R107894 {ECONEA} marine/estuarine fish study does need to be repeated. That study was classified as supplemental due to uncertainties regarding actual exposure levels during the study, and was not repairable. Refer to the DER (MRID No. 456740-03) for additional information.

The marine/estuarine acute oyster study with parent ECONEA(MRID # 456740-05) also needs to be repeated; that study was classified as supplemental as no NOEC was achieved. Therefore, the Agency needs to have acceptable Guideline studies since the results will be crucial in a quantitative risk assessment especially in determining potential risks to Endangered Species.

Request to Upgrade Fish Early Life-Stage Study to Acceptable(MRID# 456741-05):

Since the CL322250, degradate of ECONEA, will be the primary compound of concern for chronic exposure to fish, the Agency recommends that the study not be upgraded, and that a new freshwater fish early life-stage test using CL322250 (Guideline 850.1300/72-4a) be submitted.

Mysid Life-Cycle Testing for CL322248 Waiver Request:

The Agency does not have any evidence that the CL322248 metabolite will be less than the CL322250 metabolite to marine/estuarine species. The Agency recommends placing the Mysid life-cycle study(Guideline 850.1400/72-4b) in reserve, pending the results of acute testing on marine/estuarine species with the CL 322248 metabolite.

Marine/Estuarine Acute Testing for CL322248 Waiver Request:

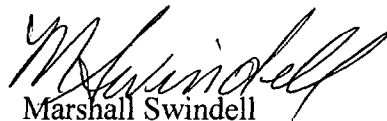
The Agency recommends that the waiver request for the three marine/estuarine species (Guideline 850.1075, 850.1025 or 1055, and 850.1035 or 1045;72-3 a,b,c) is not acceptable. Conduct acute testing with the marine/estuarine fish and one of the invertebrate species, preferably mysid; testing with the remaining species will be reserved.

A copy of the complete science review is enclosed.

The product may not be lawfully distributed in interstate commerce until the above discrepancies have been clarified.

If you have any questions concerning this letter, please contact Karen M. Leavy-Munk at (703)-308-6237.

Sincerely,



Marshall Swindell
Product Manager 33
Regulatory Management Branch I
Antimicrobial Division(7510C)



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES
June 6, 2005

MEMORANDUM

Subject: Econeal: Registrant Response to Agency Ecological Effects Review/Waiver Requests (D312744).

To: Dennis Edwards, Chief
Marshall Swindell, RM 33
Karen Leavy, PMT 33
Regulatory Management Branch I
Antimicrobials Division, 7510C

From: Kathryn Montague, Biologist
Rick Petrie, Team Leader
Risk Assessment and Science Support Branch
Antimicrobials Division, 7510C

James Breithaupt, Agronomist
Environmental Review Branch I
Environmental Fate and Effects Division, 7507C

Through: Norm Cook, Chief
Siroos Mostaghimi, Team Leader
Risk Assessment and Science Support Branch
Antimicrobials Division, 7510C

1. Bioconcentration Factor Waiver Request:

The registrant has requested that the Antimicrobial Division (AD) consider waiving the bioconcentration in fish (165-4) guideline. They cite several reasons, including a relatively low log Pow and a lack of persistence. Therefore, AD conducted some estimations of concentrations in fish using several mathematical equations and estimated water concentrations. Some of the modeling inputs and their justifications are included in Table 1, while Appendix A contains additional information.

a. Justification of Chemical Selection

The use of the Econeal degradate 322,250 and fresh water in bioconcentration modeling represents the worst case scenario of exposure and bioconcentration. Parent Econeal is not stable above pH 5, and fresh water ranges from about pH 5 to pH 7. Therefore, it is not likely to present in water for long periods of time. Parent Econeal degrades via hydrolysis to 322,250 which does not degrade by the hydrolytic process. The half-lives of parent Econeal in fresh water at 25 °C were 14, 0.35, and 0.1 days at pH values of 5, 7, and 9. The calculated half-life in salt water at 25 °C was 0.1 day. In anaerobic aquatic metabolism studies (representing sediment), Econeal and 322,250 degraded with half-lives of 29 and 31 days, respectively, but 322,250 was found mostly in the water phase instead of the sediment. The salt water half-lives were 0.7 and 22 days, respectively. In aerobic aquatic metabolism studies (representing the water column), Econeal degraded with a calculated half-life of 12.3 days in fresh water while 322,250 was stable. In salt water, the half-lives of parent Econeal and 322,250 were 0.6 and 288 days, respectively. The 322,250 compound is also more mobile than parent Econeal based on adsorption coefficients.

Another indicator of bioconcentration potential of the compound is the Log Pow. Log Pow refers to the partitioning within an octanol/water mixture. A Log Pow of <3 (Pow<1000) generally indicates low potential to bioconcentrate and is a criterion for waiving a bioconcentration study. The range of Log Pow can be from 0 to 6 (Pow of 0 to 1 million). In the case of 322,250, the maximum Log Pow of 1.66 (Pow=46) is much less than a Log Pow of 3.0 (Pow of 1,000) and indicates a limited potential to bioconcentrate.

Table 1. Bioconcentration Modeling of Econeal in Fish

Input	Value	Comments
Log Pow	1.66	For freshwater (worst case) pH 6 322,250
Log BCF Estimation Equation	$0.542 * \text{Log Pow} + 0.124$	Janssen, 1/17/05 letter $\text{BCF} = \text{Kuptake} / \text{Kdeposition}$ $= \text{K1} / \text{K2}$
Log K2 Estimation Equation	$-0.414 * \text{Log Pow} + 1.47$	OECD 305 K2=deposition rate constant
Water Concentration	0.00103	ppm Total concentration in poorly flushed harbor

b. Justification for Inputs

AD used the estimated total concentration from the MAMPEC model as the concentration to be

bioconcentrated. Where possible, information on the 322,250 metabolite was used as inputs, but parent information was used in its absence. Based on the modeling, the maximum concentration of the Econeal metabolite 322,250 is 0.011 ppm (Table 2)

Table 2. Estimation of BCF Parameters for 322,250 in Fish.

Output	Value	Comments
Time to reach 95 % of steady state (days)	3.8 2.7	Freshwater Saltwater OECD 305 3/k2 Freshwater
Concentration in fish tissue at steady state	0.011	(ppm)

Based on these results, AD agrees that no further bioconcentration testing is required for Econeal or its major metabolites, and recommends that the waiver request for bioconcentration testing in fish (165-4/850.1730) and oyster (165-4/850.1710) be granted.

2. Avian Dietary Waiver Request:

Janssen Pharmaceutica, Inc., has agreed to conduct avian dietary testing with the mallard on R107894 (Econeal) and its major metabolite CL322250. They have requested a waiver for the required avian dietary on the subsequent metabolite CL322248, a debrominated form of CL322250 which forms in salt water. Their rationale is that CL322248 should be less toxic than CL322250, and, therefore, the CL322250 endpoints should be adequate for regulatory decision-making. RASSB has the following comments on the waiver request:

There is no scientific evidence supporting the registrant's statement that CL322248 is less toxic than CL322250; no studies have been submitted on the toxicity of the CL322348 metabolite in either mammals or birds. The observation that the CL322250 metabolite is less toxic to those species than the parent compound does not indicate with any scientific validity that the next subsequent breakdown product, CL322348, will be even less toxic. Note that in aquatic studies, the CL322250 degradate is actually MORE toxic than the parent R107894; in similar aquatic studies, the toxicity of CL322248 is more comparable to, or perhaps slightly less than, the toxicity of the parent compound.

Since all of these are breakdown products of chlorfenapyr, a compound which is very highly toxic to birds, we would be remiss attempting to conduct a risk assessment without avian dietary toxicity data on all the metabolites that can result in dietary exposure to birds from the intended use of this compound. A single avian dietary test on CL322248 using the mallard will provide concrete evidence of the comparative toxicity of CL322248 vs CL322350 and R107894. Data on

all of these compounds will be of value in conducting a risk assessment for regulatory decision-making. RASSB therefore recommends that the waiver request for an avian dietary study on CL322248 be denied.

3. Request to Upgrade Sheepshead Minnow Acute Study to Acceptable (MRID #456741-01)

The registrant has submitted some additional information and a rationale for upgrading the sheepshead minnow acute study on CL322250 to acceptable. Although the study does not meet Guideline requirements (850.1075/72-1a) due to inadequate sampling of test concentrations during the study and the lack of an LC50 determination at the relatively low test concentrations tested, the study does indicate that the CL322250 metabolite is substantially less toxic than parent Econeia (R107894). Acute sheepshead minnow testing with parent Econeia resulted in an LC50 of 23.71 ppb and a NOEC of 10 ppb (MRID #456740-03, supplemental study), while the CL322250 test resulted in an LC50 > 950 ppb and a NOEC of 950 ppb. Therefore, the CL322250 marine/estuarine fish study does not need to be repeated. However, **the R107894 (Econeia) marine/estuarine fish study does need to be repeated**; this was not accurately stated in the June 1, 2004, memorandum from the Agency to the registrant. That study was classified as supplemental due to uncertainties regarding actual exposure levels during the study, and was not repairable. Refer to the DER (MRID #456740-03) for additional information. **The marine/estuarine acute oyster study with parent Econeia (MRID #456740-05) also needs to be repeated**; that study was classified as supplemental as no NOEC was achieved. These studies appear to provide the most sensitive endpoints for the marine/estuarine risk assessment for Econeia, and the Agency therefore needs to have acceptable Guideline studies since the results will be crucial in a quantitative risk assessment, especially in determining potential risks to Endangered Species.

4. Request to Upgrade Fish Early Life-stage Study to Acceptable (MRID #456741-05)

The registrant has requested that the Agency consider upgrading a freshwater fish early life-stage test with Zebra fish to acceptable or supplemental/upgradeable. The study was classified as invalid for several reasons: the use of dechlorinated tap water as dilution water, with none of the required daily testing of residual chlorine compound levels or concurrent testing on daphnids; the laboratory could not verify that organophosphorous concentrations in the Instant Ocean mix used were below EPA Guideline requirements, as the limit of detection used in the analysis was greater than the allowable limit; and multiple additional deviations from Guideline requirements. The registrants argue that the control performance in the zebra fish study indicates that the dilution water is of sufficient quality to support aquatic life. They also state chlorine analysis data should be available from the public water supplier and that water quality testing data for the laboratory should also be available; however, none of this data was submitted to the Agency. While RASSB agrees that the control hatching and post-hatch performance was acceptable in the study, residual chlorine levels could potentially cause subtle effects on control performance which could mask or enhance treatment effects, resulting in inaccurate conclusions from the study. OPP policy is to reject aquatic studies using dechlorinated tap water without the aforementioned testing. A copy of the dechlorinated tap water policy document was included with the memorandum to the registrants in June, 2004; that document provides the detailed

scientific rationale for this policy. Additionally, the tap water issue was only one of numerous deviations from Guideline requirements which resulted in the rejection of the study. These deviations, taken together, result in substantial uncertainty about the accuracy of the test results. Since the CL322250 degradate of Econeal will be the primary compound of concern for chronic exposure to fish, RASSB recommends that the study not be upgraded, and that a new freshwater fish early life-stage test using CL322250 (Guideline 850.1300/72-4a) be submitted.

5. Mysid Life-Cycle Testing for CL322248 Waiver Request

The registrant has requested a waiver for mysid life-cycle testing on the CL322248 metabolite. They will conduct this test on the CL322250 metabolite, and claim that available data show that the CL322248 metabolite is consistently less toxic than CL322250. The only aquatic toxicity data the Agency has received on the CL322248 metabolite is an acute freshwater invertebrate study, which does indicate that the CL322248 metabolite is less toxic to freshwater invertebrates than the CL322250 metabolite. However, this metabolite is only expected to form in marine sediments, and would therefore result in potential exposure to marine/estuarine species. Since no acute marine/estuarine studies have been submitted on the CL322248 metabolite, there is no evidence available to the Agency that the CL322248 metabolite will be less toxic than the CL322250 metabolite to marine/estuarine species. RASSB recommends placing the mysid life-cycle study (Guideline 850.1400/72-4b) in reserve, pending the results of acute testing on marine/estuarine species with the CL322248 metabolite.

6. Marine/Estuarine Acute Testing for CL322248 Waiver Request

The registrant has requested a waiver for the three acute marine/estuarine studies using the CL322248 metabolite. They again state that this metabolite is less toxic than the CL322250 metabolite precursor, but the Agency has not received sufficient data to justify that statement. As described above, the only aquatic toxicity data the Agency has received on the CL322248 metabolite is an acute freshwater invertebrate study, which does indicate that the CL322248 metabolite is less toxic to freshwater invertebrates than the CL322250 metabolite. However, this metabolite is only expected to form in marine sediments, and would therefore result in potential exposure to marine/estuarine species. The results of the acute marine/estuarine testing on CL322248 will also be important in deciding whether additional, chronic testing on that metabolite is required. Therefore, RASSB recommends that the waiver request for the three marine/estuarine species (Guidelines 850.1075, 850.1025 or 1055, and 850.1035 or 1045; 72-3 a,b,c) be denied. The registrant should conduct acute testing with the marine/estuarine fish and one of the invertebrate species, preferably mysid; testing with the remaining species will be reserved.

If you have any questions on the above, please contact Kathryn Montague (703-305-1243 or montague.kathryn@epa.gov).

Appendix A: MAMPEC Modeling Run for the Econeal Metabolite 322,250

MAMPEC - Result Sheet

Run : Default marina 400m poorly flushed Econeal, 322250 (Fresh water) Default Marina biocide 100 %
Version : MamPec 1.4.16
Run date : 5/16/2005 9:29:51 AM

Input

Environment : Default marina 400m poorly flushed
Compound : Econeal, 322250 (Fresh water)
Emission : Default Marina biocide 100 %
Load : 1.68E+02:g/d

Results

Total concentration in harbor

Maximum concentration : 1.03E+00 :ug/l
95 % concentration : 1.03E+00 :ug/l
Average concentration : 6.63E-01 :ug/l
Median concentration : 6.05E-01 :ug/l
Minimum concentration : 2.71E-01 :ug/l

Dissolved concentration in harbor

Maximum concentration : 3.99E-34 :ug/l
95 % concentration : 3.99E-34 :ug/l
Average concentration : 2.55E-34 :ug/l
Median concentration : 2.33E-34 :ug/l
Minimum concentration : 1.05E-34 :ug/l

Contaminant concentration on suspended solids

Maximum concentration : 2.27E+01 :ug/g dw
95 % concentration : 2.27E+01 :ug/g dw
Average concentration : 1.46E+01 :ug/g dw
Median concentration : 1.33E+01 :ug/g dw
Minimum concentration : 5.96E+00 :ug/g dw

Contaminant concentration in sediment after 1 year of use

Maximum concentration : 3.74E-01 :ug/g dw
95 % concentration : 3.74E-01 :ug/g dw
Average concentration : 2.39E-01 :ug/g dw
Median concentration : 2.19E-01 :ug/g dw
Minimum concentration : 9.80E-02 :ug/g dw

Contaminant concentration in sediment after 2 years of use

Maximum concentration : 3.74E-01 :ug/g dw
95 % concentration : 3.74E-01 :ug/g dw
Average concentration : 2.39E-01 :ug/g dw

Median concentration	: 2.19E-01	:ug/g dw
Minimum concentration	: 9.80E-02	:ug/g dw

Contaminant concentration in sediment after 5 years of use

Maximum concentration	: 3.74E-01	:ug/g dw
95 % concentration	: 3.74E-01	:ug/g dw
Average concentration	: 2.39E-01	:ug/g dw
Median concentration	: 2.19E-01	:ug/g dw
Minimum concentration	: 9.80E-02	:ug/g dw

Contaminant concentration in sediment after 10 years of use

Maximum concentration	: 3.74E-01	:ug/g dw
95 % concentration	: 3.74E-01	:ug/g dw
Average concentration	: 2.39E-01	:ug/g dw
Median concentration	: 2.19E-01	:ug/g dw
Minimum concentration	: 9.80E-02	:ug/g dw

MAMPEC - Input data sheet

Compound

Name	: Econea 322, 250	
Description	: Econea, 322250 (Fresh water)	
Molecular mass	: 327.	:g/Mol
Vapor pressure	: 1.90E-08	:Pa
Solubility	: 5.40E+01	:g/m3
Octanol-water coefficient	: 1.66E+01	:(-) Log (Pow)
Kd	: 0.00E+00	:m3/kg
Koc	: 3.93E+01	:(-) Log(Koc), Koc expressed as l/kg OrganicCarbon
Henry's coefficient	: 3.52E-10	:Pa.m3/mol
Melting temperature	: 252.0	:oC
pKa	: 7.08	:(-)
in water		
Biological degradation rate	: 0.00E+00	:1/d
Hydrolytic degradation rate	: 0.00E+00	:1/d
Photolytic degradation rate	: 0.00E+00	:1/d
in sediment		
Biological degradation rate	: 2.20E-02	:1/d
Hydrolytic degradation rate	: 0.00E+00	:1/d
Photolytic degradation rate	: 0.00E+00	:1/d

Environment

Description	: Default marina 400m poorly flushed	
Silt concentration	: 35.0	:g/m3
Particular organic carbon conc	: 1.0	:g Organic Carbon/m3
Dissolved organic carbon conc	: 2.0	:g/m3
Temperature	: 15.0	:oC
Salinity	: 3.40E+01	:s.e.
Depth well-mixed sediment top layer	: 1.00E-01	: m
Sediment density	: 1.000E+03	:kg/m3

Fraction organic carbon in sediment	: 3.00E-02	:kg/m3
Nett sedimentation velocity	: 1.00E+00	:m/d
pH	: 8.0	:(-)
Background concentrations	: 0.00E+00	:ug/l
Length of river, not part of harbor (x1)	: 400	:m
Length of harbor (y1) (Å river or coast)	: 400	
Width of harbor (x2)(// river or coast)	: 400	:m
Width of river (y2)	: 400	:m
Depth of harbor	: 3.5	:m
Length of open harbour mouth (x3)	: 50	:m
Flow	: 0.2	:m/s
Flow of flushing into harbor	: 0	:m3/s
Tidal height	: 0	:m
Density difference	: 0	:kg/m3
Density difference flushing	: 0	:kg/m3
Tidal period	: 12.41	:h
Exchange surface	: 175	:m2
Depth at harbour mouth	: 3.5	:m
Height underwater dam at mouth	: 0	:m
Width underwater dam at mouth	: 0	:m
Length selected area	: 0	:m
Width selected area	: 0	:m
Depth selected area	: 0	:m
Flow	: 0	:m/s
Exchange volume in 1 tidal period	: 9954.6	:m3

Emission

Description	: Default Marina biocide 100 %
Load	: 168.1875 :g/d
Loading due to moving ships	: 0 :g/d
Loading due to ships at berth	: 168.1875 :g/d
Leaching rate ships at berth	: 2.5 :ug/cm2/d
Leaching rate ships at berth	: 2.5 :ug/cm2/d
Number of ships at berth (Class 1)	: 0
Number of ships at berth (Class 2)	: 299
Number of ships at berth (Class 3)	: 0
Number of ships at berth (Class 4)	: 0
Number of ships at berth (Class 5)	: 0
Number of ships at berth (Class 6)	: 0
Number of ships at berth (Class 7)	: 0
Number of ships at berth (Class 8)	: 0
Number of ships at berth (Class 9)	: 0
Number of ships at berth (Class 10)	: 0
Number of moving ships (Class 1)	: 0
Number of moving ships (Class 2)	: 0
Number of moving ships (Class 3)	: 0
Number of moving ships (Class 4)	: 0
Number of moving ships (Class 5)	: 0
Number of moving ships (Class 6)	: 0
Number of moving ships (Class 7)	: 0
Number of moving ships (Class 8)	: 0
Number of moving ships (Class 9)	: 0

Number of moving ships (Class 10)	: 0	
Application factor (Class 1)	: 0	:%
Application factor (Class 2)	: 100	:%
Application factor (Class 3)	: 0	:%
Application factor (Class 4)	: 0	:%
Application factor (Class 5)	: 0	:%
Application factor (Class 6)	: 20	:%
Application factor (Class 7)	: 20	:%
Application factor (Class 8)	: 20	:%
Application factor (Class 9)	: 20	:%
Application factor (Class 10)	: 20	:%
Underwater ship area (Class 1)	: 20	:m2
Underwater ship area (Class 2)	: 22.5	:m2
Underwater ship area (Class 3)	: 450	:m2
Underwater ship area (Class 4)	: 3061	:m2
Underwater ship area (Class 5)	: 5999	:m2
Underwater ship area (Class 6)	: 9917	:m2
Underwater ship area (Class 7)	: 14814	:m2
Underwater ship area (Class 8)	: 22645	:m2
Underwater ship area (Class 9)	: 27547	:m2
Underwater ship area (Class 10)	: 39668	:m2
Ship Length (Class 1)	: 0-10	:m
Ship Length (Class 2)	: 10-50	:m
Ship Length (Class 3)	: 50-100	:m
Ship Length (Class 4)	: 100-150	:m
Ship Length (Class 5)	: 150-200	:m
Ship Length (Class 6)	: 200-250	:m
Ship Length (Class 7)	: 250-300	:m
Ship Length (Class 8)	: 300-350	:m
Ship Length (Class 9)	: 350-400	:m
Ship Length (Class 10)	: > 400	:m

Appendix B. BCF Modeling Spreadsheet

Bioconcentration of Ectonea using Equations in OECD TG 305			
Depuration Constant Calculations (EQN 1, p. 17 of 23)			
Depuration is the removal of a pesticide by either metabolic degradation or excretion			
K2 is depuration rate constant			
Input/Formula	Value	Comment/Reference	
Log K2=-0.414 *Log Pow+1.47		OECD TG 305	
log BCF=0.542*log Pow + 0.124		Janssen, 1/17/05	
log BCF	1.02	calculated based on formula in Janssen Pharmaceutical, 1/17/05	
BCF	11	calculated	
log k2	0.783	OECD 305	
Log (10) Pow	1.66	for 322,250 and pH 6, assumes fresh water	
K2 (real scale)	6.1	10^B11 (OECD 305)	
BCF	11	11X, predicted for bluegill sunfish	
K1 (calculated)	64	K1, based on 11X bioconcentration factor	
Water Concentration	0.00103	ppm, pH 6, CHD 851/01-1073	
Time to reach 95 % of steady state	3.83	days, assuming 3 (for 95 % uptake)/ log k2 (OECD 305)	
Results			
Concentration in Fish (ppm)	Total Concentration in Water (ppm) from MAMPEC	Time (days)	
0.011	0.00103	1	
0.011	0.00103	2	
0.011	0.00103	3	
0.011	0.00103	4	
0.011	0.00103	5	
0.011	0.00103	6	
0.011	0.00103	7	
0.011	0.00103	8	
0.011	0.00103	9	
0.011	0.00103	10	
0.011	0.00103	11	
0.011	0.00103	12	
0.011	0.00103	13	
0.011	0.00103	14	
0.011	0.00103	15	
0.011	0.00103	16	
0.011	0.00103	17	
0.011	0.00103	18	
0.011	0.00103	19	
0.011	0.00103	20	
0.011	0.00103	21	
0.011	0.00103	22	

0.011	0.00103	23
0.011	0.00103	24
0.011	0.00103	25
0.011	0.00103	26
0.011	0.00103	27
0.011	0.00103	28
0.011	0.00103	29
0.011	0.00103	30
0.011	0.00103	31
0.011	0.00103	32
0.011	0.00103	33
0.011	0.00103	34
0.011	0.00103	35
0.011	0.00103	36
0.011	0.00103	37
0.011	0.00103	38
0.011	0.00103	39
0.011	0.00103	40
0.011	0.00103	41
0.011	0.00103	42
0.011	0.00103	43
0.011	0.00103	44
0.011	0.00103	45



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

May 4, 2005

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

JANSSEN PHARMACEUTICA INC.
1125 TRENTON-HARBOURTON RD
TITUSVILLE, NJ 08560-0200

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your submittal of 04-MAY-05. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your submittal was found to be in full compliance with the standards for submission of data contained in PR Notice 86-5. A copy of your bibliography is enclosed, annotated with Master Record ID's (MRIDs) assigned to each document submitted. Please use these numbers in all future references to these documents. Thank you for your cooperation. If you have any questions concerning this data submission, please raise them with the cognizant Product Manager, to whom the data have been released.

**465451-00**

May 9, 2005

Document Processing Desk (7504C)
Regulatory Management Branch I
Antimicrobial Division (7510W)
U.S. Environmental Protection Agency
1801 Bell Street
Arlington, VA 22202-4501

SUBJECT: ECONEA Technical (43813-ET)

Attn: Mr. Marshall Swindell
Product Manager 33

Enclosed are three copies of each of the following study:

Volume 1 R107894: Evaluation of the Ambient Temperature Storage Stability
Janssen Report No. AGR 458
Covance Laboratories Ltd Report Number 1073/63-D2149
May 6, 2005
OPPTS Guideline Number 830.6317 & 830.6320

MRID 46545101

This study fills the current data gap for a one-year storage stability/corrosion study.
Please submit the ECONEA product chemistry for scientific review.

Sincerely,

William R. Goodwine
Senior Director
Plant & Material Protection Division
(609) 730-2607



465394-00

May 2, 2005

Document Processing Desk (7504C)
Regulatory Management Branch I
Antimicrobial Division (7510W)
U.S. Environmental Protection Agency
1801 Bell Street
Arlington, VA 22202-4501

SUBJECT: ECONEA Technical (43813-ET)

Attn: Mr. Marshall Swindell
Product Manager 33

Enclosed are three copies of each of the following study:

Volume 1 R 107894 Primary Eye Irritation Study in Rabbits
Janssen Report No. AGR 1130
Product Safety Laboratories Project Number 17342
April 27, 2005
OPPTS Guideline Number 870.2400.

MRID 46539401

This study fills the data gap in the acute toxicity package which is now ready for scientific review.

Sincerely,

William R. Goodwine
Senior Director
Plant & Material Protection Division
(609) 730-2607



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

May 12, 2005

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

JANSSEN PHARMACEUTICA INC.
1125 TRENTON-HARBOURTON RD
TITUSVILLE, NJ 08560-0200

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your submittal of 11-MAY-05. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your submittal was found to be in full compliance with the standards for submission of data contained in PR Notice 86-5. A copy of your bibliography is enclosed, annotated with Master Record ID's (MRIDs) assigned to each document submitted. Please use these numbers in all future references to these documents. Thank you for your cooperation. If you have any questions concerning this data submission, please raise them with the cognizant Product Manager, to whom the data have been released.



January 17, 2005

FILE COPY

Mr. Marshall Swindell
Product Manager 33
Regulatory Management Branch I
Antimicrobial Division (7510W)
U.S. Environmental Protection Agency
1801 Bell Street
Arlington, VA 22202

SUBJECT: ECONEA Technical (43813-ET)
Comments on AD letter of June 1, 2004
Ecological Effects Review

We would like to address our response to EPA's deficiency letter of June 1, 2004 separately for 1) studies requested to be repeated and 2) additional new studies.

Repeat studies

Janssen agrees to repeat most of these studies and is requesting reconsideration for two studies with additional information. Using the summary tables on pages 16-18 of EPA's letter as a guide, I have created a similar overview for the outcome of our assessment for the "repeat" studies. At this time, all of the studies indicated as "repeat" in the tables below have been scheduled, with some being in the experimental phase of testing.

STUDY	SPECIES	STATUS
ECONEA: Janssen code no.R107894 (=AC303,268)		
FW-fish acute-850.1075	bluegill	repeat
FW-fish acute-850.1075	rainbow trout	repeat
FW invert acute-850.1010	daphnid	repeat
FW invert life cycle 850.1300	daphnid	repeat
Green algae - 850.5400	<i>Selenastrum capricornutum</i> ¹	repeat
Marine diatom - 850.5400	<i>Skeletonema costatum</i>	repeat

¹Note: *Selenastrum capricornutum* also known as *Raphidocelis subcapitata*.



STUDY	SPECIES	STATUS
CL322,250 metabolite		
FW-fish acute-850.1075	bluegill	repeat
FW-fish acute-850.1075	rainbow trout	repeat
FW invert acute-850.1010	daphnid	repeat
FW fish ELS - 850.1400	zebra fish	Reconsideration ²
FW invert life cycle 850.1300	daphnid	repeat
ME fish acute - 850.1075	Sheepshead minnow	Reconsideration ²
Marine diatom - 850.5400	<i>Skeletonema costatum</i>	repeat

²Note: Comments provided separately as appendices.

Additional Requirements:

Prior to submitting the file for ECONEA antifoulant, our scientists carefully reviewed all available information on the active ingredient and metabolites before deciding that most of the additional testing being proposed by USEPA in its letter of June 1, 2004 was not necessary. I think it would be useful to review our thought process and ask USEPA to consider this rationale for waiver requests for the pertinent studies:

▪ Avian acute oral studies for metabolites CL322250 & CL322248

Janssen proposes to waive the avian acute oral toxicity tests for both metabolites. Historically, it has been assumed that acute toxicity in avian species (classically northern bobwhite, mallards and Japanese quail) closely mimics the acute toxicity to mammals (classically rats and mice). Without reference to specific test substances, a rough estimate of the validity of this assumption was made by Wildlife International Ltd, at Janssen's request, by enumerating the number of acute LD50 studies that had to be repeated (the most common cause for a repeat study being the inability to calculate an LD50 due to excessive or insufficient mortality). In 1,107 avian acute oral LD50 studies conducted over the past 27 years, the reported toxicity of the test substance to mammals has been sufficiently close to accurately predict the test dosages needed to establish the LD50 value 1,050 times (failure rate ~ 5%). This is over various classes of material and modes of action. It can be seen that, in the vast majority of cases, the mammalian LD50 value was predictive of the avian LD50 value.

With regard to acute oral toxicity studies in rat, the ECONEA metabolites are markedly less toxic than the parent compound. Specifically, the LD50 for CL325195 is 25 X higher than for R107894, while CL322250 is 83 times less toxic than the parent molecule. An acute oral toxicity study was not performed on metabolite CL322248 (a further degradation product of CL322250) because the weight of evidence indicates that CL322248 is less toxic than its precursor. On avian species, data are available on both mallard duck and bobwhite quail for both parent compound and metabolite CL325,195. Referring back to the mammalian (rat) acute oral toxicity rat data, since CL325,195 is the



most toxic of the three metabolites the avian acute data for CL325,195 can be used in a screening level risk assessment for the other metabolites.

Acute Oral Toxicity LD50 (mg/kg)				
Compound	Mallard duck	Bobwhite quail	Rat - male	Rat - female
R107894	77	25	27.0	29.9
CL325195	741	> 2,250	776	1,367
CL322250	-	-	> 5,000	2,500
CL322248	-	-	-	-

▪ Avian dietary – R107894

Although this data requirement was not listed on some earlier draft guidance documents obtained from EPA for antifoulants specifically, it is listed under general requirements for aquatic non-food use patterns in 40 CFR. Janssen has already initiated this study. This should highlight the urgent need to codify the new 158 guidelines for antimicrobials, including antifoulants and wood preservatives. Without clear guidance on data requirements, data gaps will be a common occurrence.

▪ Avian Dietary – Metabolites CL322250 and CL322248

Janssen agrees to perform the avian dietary study on mallard with metabolite CL322250. However, considering the weight of evidence that CL322248 is of equal or lesser toxicity than its precursor CL322250, Janssen believes that the toxic end-points from CL322,250 can be used for screening level risk assessments for CL322,248. Additional studies on CL322248 will be of limited value for regulatory decision-making.

▪ Fish Bioaccumulation (BCF) study for R107894 (parent):

Janssen agrees in principle to conduct a fish BCF study with R107894, however, a number of technical difficulties have been identified. EPA guidance and protocol approval will be necessary before proceeding.

The octanol/water partition coefficient for parent molecule R107894 ($\log P = 3.5$) was conducted at pH 5 because of the instability of the molecule in water at higher pH levels. The hydrolysis data indicates that ECONEA will degrade rapidly under the tests conditions (temperature, pH, duration) required for both the fish and oyster BCF studies. The half-life of ECONEA in freshwater (pH 7, 25°C) and seawater (pH 8, 25°C) is 8 and 3 hours, respectively. At pH 7 (25°C), the major transformation products detected were CL322,250 and CL322,248, with maximum concentrations of 68% and 30%, respectively, of the applied dose observed on day 7 and day 30. Only 28% and 9.8 % of the parent compound was recovered after only 12 and 24 hours. Degradation in seawater was even more rapid, with 2.2% ECONEA recovered at 12 hours; parent compound was not detected from 24 hours onward. The major transformation product detected was



CL322,250 with a maximum concentration of 96% on day 21; CL322,248 was not detected at any sampling interval.

The 96h-LC50 for rainbow trout and bluegill sunfish is 1.49 µg/L and 6.94 µg/L, respectively. The guidelines recommend testing with bluegill sunfish at concentrations of 1/100 and 1/1000 of the LC50, and below the aqueous solubility (0.16 mg/L). Thus, the exposure concentrations should be 69 ng/L and 6.9 ng/L for bluegill sunfish and 14.9 ng/L and 1.49 ng/L for rainbow trout.

Technically, the fish BCF study conducted at pH 7 and 20-25°C should be feasible in a flow through system with a turnover rate every 4 hours, however, a significant amount of the applied R107894 will be converted to metabolite CL322,250 to the extent that recoveries of parent molecule will likely fall below required recoveries of 70% using cold analytical methods. Using the phenyl labeled radiochemical, (which has a supplied specific activity of 75.4 µCi.mg⁻¹), the highest concentration would result in tank water activity levels of 5000 dpm.L⁻¹, which are detectable, however, the total radioactivity in the water at 6.9 ng.L⁻¹ would not.

A theoretical bioconcentration factor of about 105 was estimated for R107894. This was calculated using a relatively standard correlation between the octanol:water partition coefficient and measured bioconcentration factor. The calculation used was [\log_{10} of BCF = $0.542 \times \log_{10} K_{ow} + 0.124$]; taken from Branson, et al (1975) In "Structure Activity Correlations in Studies of Toxicity and Bioaccumulation with Aquatic Organisms" Veith GD and Konasewich (eds). This relationship for predicting bioconcentration factors is referred to in the ASTM E-1022-84 method as referenced within the OECD and OPPTS 850.1730 guidelines for fish bioaccumulation studies. Using the BCF of 105, further optimization techniques for the detection of parent and metabolite(s) residues in fish, particularly during depuration, will be necessary (i.e. analysis of whole tissues in the depuration phase without replication).

▪ Oyster Bioaccumulation (BCF) study for R107894 (parent):

In seawater, it is not technically possible even in a flow through system to maintain levels of parent compound with such a rapid hydrolysis rate. Referring to the mysid chronic flow through study performed with parent compound (MRID (45674009), the levels of R107894 recovered analytically was 28-43% of the nominal, while the recovery of CL322250 was 39-53% of the nominal R107894 concentration. The compound to which the oyster will be primarily exposed is the major metabolite CL322,250. Since the Log P of CL322,250 is 0.65, CL322,250 is not likely to bioaccumulate. Janssen believes this test should be reserved, pending the outcome of the fish BCF study.



▪ Bioaccumulation (BCF) studies for metabolites CL322,250 and CL322,248

Janssen proposes to waive tests on metabolite CL322,250 based on Log P values less than one (1) at pH 7 and 8 which are relevant for freshwater and seawater conditions, respectively. The partition coefficients for parent and all three metabolites are summarized in the table below. Low Log P values (<3.0) are predictive of compounds with a low tendency to bioaccumulate.

Compound	Log P (measured)			
	PH - 5	PH - 6	PH - 7	PH - 8
ECONEA (parent)	3.5	NA	NA	NA
CL325,195 (metabolite)	NA	2.20	1.80	0.88
CL322,250 (metabolite)	NA	1.66	1.0	0.55
CL322,248 (metabolite)	NA	1.23	0.5	0.005

NA – not available

▪ Mysid Life Cycle for Metabolites CL322,250 and CL322,248

Mysid life cycle for CL322,250 and CL322,248 – Janssen agrees that a mysid life cycle study should be conducted for CL322,250 since this is the major degradate from hydrolysis and aerobic and anaerobic degradation pathways. Regarding CL322,248 testing, since the available data consistently shows that this compound is no more toxic than its precursor CL322,250, the toxic endpoints for CL322,250 can be used in the initial screening level risk assessments for CL322,248. For example, both metabolites are of comparable toxicity to the freshwater invertebrate *Daphnia magna* in (chronic) reproduction studies.

▪ Aquatic toxicity studies with CL322,248 in marine species

After some initial aquatic toxicity tests were performed with CL322,248, it became readily apparent that the toxic endpoints of CL322,248 were comparable to its precursor CL322,250. For screening level risk assessments, Janssen believes that the toxic endpoints from CL322,250 can be used for CL322,248; additional studies on CL322,248 will be of limited value for regulatory decision making. Secondary metabolite CL322,248 is not a hydrolysis product of ECONEA in seawater, and is only a by-product of metabolism associated with aerobic and anaerobic sediment systems.

JANSSEN



PHARMACEUTICA INC.

Janssen Pharmaceutica would like to arrange a meeting with the RASSB scientists within Antimicrobial Division to discuss these waiver request rationales. I would like to coordinate this ECONEA ecological effects meeting with a meeting on toxicology (requested in my letter of December 13, 2004). I would propose that these two meetings be held on consecutive days, preferably an afternoon meeting on the first day followed by a morning meeting the following day in mid to late February 2005. I will be in touch by phone to discuss appropriate scheduling.

I can be reached by phone directly at (609) 730-2607 if any questions.

Sincerely,

William R. Goodwine
Senior Director
Plant & Material Protection Division
Tel: (609) 730-2607
Fax: (609) 730-2411
bgoodwi@janus.jnj.com

Appendix A



**SPRINGBORN SMITHERS
LABORATORIES**

790 Main Street • Wareham, MA 02571-1075

Phone: (508) 295-2550 • Fax: (508) 295-8107

July 19, 2004

William Goodwine
Janssen Pharmaceutica
1125 Trenton-Harbourton
Titusville, NJ 08560

RE: Response to the DER regarding the sheepshead minnow flow-through acute study with CL 322,250 (MRID No.: 456741-01)

Dear Bill:

We have reviewed the DER regarding the Sheepshead minnow flow-through acute study with CL 322,250 (MRID No: 456741-01) and have provided our comments on the DER below for your consideration. The EPA-EFED reviewer had one significant concern with this study – no LC50 was achieved and testing was not conducted at high enough levels for the non-specific endpoint to be adequate for risk assessment.

It may be useful in the review of the CL 322,250 sheepshead minnow acute test to consider that CL 322,250 is the hydrolysis product of R107894 and that the sheepshead minnow LC50 and NOEC for R107894 were 0.026 and 0.010 mg/L, respectively. The R107894 acute study was conducted under flow-through conditions and the exposure solutions were essentially half of the nominal concentrations due to rapid hydrolysis of R107894 to CL 322,250. The results from the CL 322,250 sheepshead minnow LC50 study demonstrate the LC50 of CL 322,250 is at least 3.7 times greater than the LC50 of the parent material and the NOEC is at least 9.5 times greater than the NOEC of the parent material. The CL 322,250 sheepshead minnow acute study also demonstrates that the presence of CL 322,250 in the R107894 study did not contribute to the toxicity of R107894 to sheepshead minnows.

The EPA-EFED reviewer suggested that this study should have been conducted at higher concentrations. However, one of their points in defense of testing higher was inaccurate and may have some bearing on the study acceptability. The review suggested that Hogland's medium was the same medium used in the sheepshead minnow study. However Hogland's medium is an acidic freshwater nutrient solution used for culturing *Lemna gibba* and other aquatic plants. The ionic concentration and hydrogen ion concentration of Hogland's medium is orders of magnitude less than the 32 parts per thousand seawater used in the sheepshead minnow exposure and is not an acceptable medium for this species. We often see significant differences in the solubility of a test substance between different matrices.

Another limiting factor for testing at higher concentrations of CL 322,250 in water is its limited solubility in organic solvents. The solubility of CL 322,250 in both acetone and DMF is approximately 10 mg/mL, which limits testing under flow-through conditions to concentrations

of 1 mg/L or less in water due to the maximum solvent concentration of 100 μ L/L in water. The reviewer noted that analytical recovery samples in Hogland's medium were fortified at 2 mg/L. However, this sample was fortified using significantly higher solvent concentrations than the Agency allows in aquatic toxicity testing and using a solvent (acetonitrile), which is not recommended as a carrier in aquatic toxicity tests. A saturator column was not employed because the stability of CL 322,250 was not known at the time of testing, but was suspected of being somewhat unstable in water, thus the studies were conducted under flow-through conditions.

The EPA-EFED reviewer also identified additional guideline deviations that were of concern in this study.

1. The Guideline states that the test substance should be measured in each replicate at 0, 48 and 96 hours. In the Study Report, concentrations were not reported for each replicate (a mean value was reported for each set of replicates) and were only measured at the start (0 hours) and end of the test (96 hours).

Unfortunately, the Draft OPPTS Guidelines can be contradictory, which is the basis of this comment. The OPPTS 850.1075 Draft Guideline does require that analyses be conducted on each replicate and at 0, 48 and 96 hours to confirm the exposure. However, the OPPTS 850.1000 Draft Guideline requires analysis at 0 hour and 96 hour, but the 48-hour analysis is only necessary if there is concern for stability or variability. The pre-test analysis conducted in this study demonstrated that the flow-through conditions were adequate to assure stability and acceptable variability, thus making the 48-hour analysis unnecessary. The OPPTS 850.1000 Draft Guideline also allows for analysis of alternating replicates when a splitter box is used in a flow-through study. A splitter box was used in this system to deliver exposure solutions to each replicate therefore making analysis of each replicate at each sampling interval unnecessary.

2. No details were provided on when the fish were added to the test chamber in relation to the addition of the test substance. Also, the Study Report does not indicate if any disease treatment was administered to the fish 48 hours prior to test initiation or during the test.

On page 13 of the Study Report it states that the diluter system was in operation for 10 days prior to initiation of the definitive exposure to allow equilibration of the test substance in the diluter apparatus and exposure vessels. Although not explicitly stated in the Study Report, there was no disease treatment administered to the fish 48 hours prior to testing initiation or during the test. This is verified in the raw data.

3. Information pertaining to acclimation of the fish (disease treatment, pretest mortality, water temperature) was not provided.

As stated above, there was no disease treatment to this fish population. On page 11 of the Study Report it states that there was no mortality in the fish population for 48 hours prior to test

initiation and that the fish were held at a water temperature range of 22 to 24 °C for 14 days prior to test initiation.

The EPA-EEFD reviewer also identified several additional guideline deviations. Only those deviations not already cited above are addressed below.

* The Guideline specifies that temperature should be recorded at least hourly in one replicate throughout the test. The Study Report indicates that continuous temperature monitoring was performed in replicate A of the control but no hourly measurements were reported.

In this study a minimum-maximum thermometer was used to monitor temperature continuously in replicate A of the control. This thermometer was read daily and reset. Therefore, the range reported for each day was the minimum and maximum range for each day. In our opinion, we have exceeded the guideline requirement of hourly measurements by recoding the temperature continuously. However, using this technique we are only able to provide the temperature range over a 24-hour period, which for this study was 22 to 23 °C compared to the guideline range of 20 to 24 °C.

* The Guideline states that no more than 25% variation is allowed between test concentrations within the same treatment during the test. Since concentrations were only measured at start of test (0 hours) and at end of test (96 hours) and in alternate replicates, it cannot be determined whether this requirement was met during the test.

As stated above, the analytical sampling intervals and alternating replicate analysis follows the OPPTS 850.1000 Draft Guideline. In addition, the OPPTS 850.1000 Draft Guideline states, "to the extent possible, variability in measured concentrations should be minimized. The goal for limiting variability of measurements between replicates of the same concentration and over time in the same concentration, is maintaining the ratio of the highest concentration to the lowest concentration at 1.5:1 or less." The variability in the exposure analysis from this study easily meets this requirement. Also, based on the analytical data presented in Table 2 of the Study Report and our extensive experience in conducting flow-through acute exposure, we are confident that we met the 25% variation requirement as well.

* Information regarding the test substance, such as substance form, impurities, and physicochemical characteristics, was not provided.

It is generally the responsibility for the Study Sponsor to provide this information.

* It could not be determined whether the light intensity measurement was within the recommended intensity range specified in the Guideline since the units, lux can only be converted to lm/m² and the recommendation is in lm.

If you take into consideration the surface area of the aquarium (30 x 15 cm or 0.045 m²), the Lumen's over the aquarium surface ranged between 34 and 39, which is within the 30 to 100 lm range recommended in the Guideline.

We hope that these responses to the EPA-EEFD reviewer's comments will assist in further evaluating this study and allow for a reconsideration of this studies classification. We would also be happy to provide any additional information regarding this study at the request of the Agency.

Best regards,

Ronald C. Biever
Director, Environmental Toxicology

Appendix B

**RE: Response to DER regarding fish early life stage toxicity test of CL322,250:
Danio rerio (Report No. WE-05-005, Janssen Report No. AGR 290)
MRID 45674105**

1. The basis for rejection of this study is that tap water was used as the basis for the demineralization water used as dilution water and that daily chlorine analysis were not conducted. Also, the total organophosphorus concentrations in the Instant Ocean mix were not verified to be less than the recommended maximum concentration of 50 ng/L. The underlying issue in both cases is the concern that the water cannot support aquatic life.

OPPTS guideline 850.1400 is based on OECD guideline 210, which is consistent with 40 CFR 797.1600 and OPP 72-4. OECD 210 makes allowance for the use of tap water for these tests. The laboratory that has conducted this study (LISEC) has performed these and other tests for more than 10 years without any adverse effect on the survivability of aquatic organisms. In addition, tap water is routinely used for the maintenance of the fish, brood of *Daphnia* (ISO 6341), and for culture of algae (M2). Historical control data can be provided as evidence that the tap water used can support aquatic life. While daily chlorine analysis was not performed, chlorine analysis should be available from the public supplier to document chlorine levels during the test period. In addition, water quality at LISEC is tested on a regular basis by an external control organization and these records should also be attainable. Individual organochloro and organophosphorous pesticides were analyzed in the Instant Ocean mix (all less than the LOD of the analytical method), however, the total could not be verified to be less than 50 ng/L Organophosphates

OPPTS850.1400 stipulates, "*any water in which the test species shows control survival, at least as good as described in Table 4...is suitable as a test water*". The study complies with this criteria, which for *Danio rerio* (zebra fish) controls, is 87% post-hatch success in this study versus the guideline criteria of 70%. The hatching success in the controls was 87% (the guidelines are silent on establishing a acceptable level for hatching success for this species). It is clear that the water used unequivocally does support aquatic life and is suitable water as defined in the guidelines.

Referring to OECD Guideline 202 (draft), "*Glass-distilled or carbon-filtered deionized water with a conductivity of less than 10 μ S/cm is acceptable as the diluent for making reconstituted water*". The conductivity of the carbon-filtered deionized water at LISEC is always around 0.2 μ S/cm (maximum of 2 μ S/cm). This information can be added by a report amendment.

The reviewers cited other minor deviations to the OPPTS 850.1400 guidelines that did not affect the test results. These can be addressed, if necessary, should EPA agree to reclassify the study as upgradable.

DATA PACKAGE BEAN SHEET

Date: 05-Aug-2005

Page 1 of 1

***** Registration Information *****

Registration: 43813-ET - ECONEA TECHNICAL

Company: 43813 - JANSSEN PHARMACEUTICA INC.

Risk Manager: RM 33 - Marshall Swindell - (703) 308-6341 Room# CM-2 308H

Risk Manager Reviewer: Karen Leavy KLEAVY

Sent Date: 04-May-2005

Calculated Due Date: 08-Jan-2007

Edited Due Date: _____

Type of Registration: Product Registration - Section 3

Action Desc: (A41) NEW AI;NON-FOOD USE;OUTDOOR;OTHER USES;

Ingredients: 119093, 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-(93.2%)

***** Data Package Information *****Expedite: ☐ Yes ☒ No

Date Sent: 06-May-2005

Due Back: _____

DP Ingredient: 119093, 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-

DP Title: _____

CSF Included: ☒ Yes ☐ NoLabel Included: ☒ Yes ☐ No

Parent DP #: _____

Assigned To**Date In****Date Out**

Organization: AD / RASSB

11-May-2005

09-Jun-2005

Last Possible Science Due Date: 03-Jul-2006

Team Name: RASSB2

11-May-2005

09-Jun-2005

Science Due Date: _____

Reviewer Name: McMahon, Timothy

11-May-2005

09-Jun-2005

Sub-Data Package Due Date: _____

Contractor Name: _____

***** Studies Sent for Review ********** Additional Data Package for this Decision ********** Data Package Instructions *****

Please review the following acute toxicity studies submitted in support of registration of the new chemical ECONEA. Acute oral(MRID No. 456739-20), Acute oral(Fixed Dose Procedure) in rats(MRID No. 456739-15), Acute Dermal Toxicity(LD50) test in Rats(MRID No. 456739-16), Acute Inhalation toxicity study in Rats(MRID No. 4456739-17), Acute Dermal Irritation in Rabbits(MRID No. 456739-18), Buehler Test in Guinea Pigs for Delayed Skin Sensitisation Potential(MRID No. 456739-19), and Primary Eye Irritation Study in Rabbits(MRID No. 465394-00), copy of proposed labeling, and CSF. Action Code A41, PRIA, Attn: Tim McMahon

DATA PACKAGE BEAN SHEET

Date: 04-Aug-2005

Page 1 of 1

***** Registration Information *****

Registration: 43813-ET - ECONEA TECHNICAL

Company: 43813 - JANSSEN PHARMACEUTICA INC.

Risk Manager: RM 33 - Marshall Swindell - (703) 308-6341 Room# CM-2 308H

Risk Manager Reviewer: Karen Leavy KLEAVY

Sent Date: 04-May-2005

Calculated Due Date: 08-Jan-2007

Edited Due Date: _____

Type of Registration: Product Registration - Section 3

Action Desc: (A41) NEW AI;NON-FOOD USE;OUTDOOR;OTHER USES;

Ingredients: 119093, 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-(93.2%)

***** Data Package Information *****Expedite: ☐ Yes ☒ No

Date Sent: 06-May-2005

Due Back: _____

DP Ingredient: 119093, 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-

DP Title: _____

CSF Included: ☒ Yes ☐ NoLabel Included: ☒ Yes ☐ No

Parent DP #: _____

Assigned To**Date In****Date Out**

Organization: AD / RASSB

11-May-2005

Last Possible Science Due Date: 03-Jul-2006

Team Name: RASSB2

11-May-2005

Science Due Date: _____

Reviewer Name: McMahon, Timothy

11-May-2005

Sub-Data Package Due Date: _____

Contractor Name: _____

***** Studies Sent for Review ********** Additional Data Package for this Decision ********** Data Package Instructions *****

Please review the following acute toxicity studies submitted in support of registration of the new chemical ECONEA. Acute oral(MRID No. 456739-20), Acute oral(Fixed Dose Procedure) in rats(MRID No. 456739-15), Acute Dermal Toxicity(LD50) test in Rats(MRID No. 456739-16), Acute Inhalation toxicity study in Rats(MRID No. 4456739-17), Acute Dermal Irritation in Rabbits(MRID No. 456739-18), Buehler Test in Guinea Pigs for Delayed Skin Sensitisation Potential(MRID No. 456739-19), and Primary Eye Irritation Study in Rabbits(MRID No. 465394-00), copy of proposed labeling, and CSF. Action Code A41, PRIA, Attn: Tim McMahon

Al you must Nader or Norm Cook to close
this bean before you can close the
Submission. Marshall

DATA PACKAGE BEAN SHEET

Date: 15-Jun-2005

Page 1 of 1

***** Registration Information *****

Registration: 43813-ET - ECONEA TECHNICAL

Company: 43813 - JANSSEN PHARMACEUTICA INC.

Risk Manager: RM 33 - Marshall Swindell - (703) 308-6341 Room# CM-2 308H

Risk Manager Reviewer: Karen Leavy KLEAVY

Sent Date: 12-May-2005

Calculated Due Date: 08-Jan-2007

Edited Due Date: _____

Type of Registration: Product Registration - Section 3

Action Desc: (A41) NEW AI;NON-FOOD USE;OUTDOOR;OTHER USES;

Ingredients: 119093, 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-(93.2%)

***** Data Package Information *****Expedite: ☐ Yes ☒ No

Date Sent: 15-Jun-2005

Due Back: _____

DP Ingredient: 119093, 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-

DP Title: _____

CSF Included: ☒ Yes ☐ NoLabel Included: ☒ Yes ☐ No

Parent DP #: _____

Assigned To**Date In****Date Out**

Organization: AD / PSB

Last Possible Science Due Date: 03-Jul-2006

Team Name: CTT

Science Due Date: _____

Reviewer Name: _____

Sub-Data Package Due Date: _____

Contractor Name: _____

***** Studies Sent for Review ********** Additional Data Package for this Decision ********** Data Package Instructions *****

Please review the product Chemistry data submitted in support of registration for the new a.i., ECONEA. Stability/Corrosion study(MRID No. 465451-01); Physical Chemistry(MRID No. 456739-07; Product ID & Composition(MRID No. 456958-01), Description of Materials(MRID No. 456958-02), Formation of Impurities(MRID No. 456739-01);Preliminary Analysis(MRID No. 456739-02); Preliminary Analysis(MRID No. 456739-03); Preliminary Analysis(MRID No. 456739-04); Physical/Chem. Charac.(MRID No. 456739-05);Physical/Chem. Charac.(MRID No. 456739-06); Action Code A41; PRIA

DATA PACKAGE BEAN SHEET

Date: 06-May-2005

Page 1 of 2

***** Registration Information *****

Registration: 43813-ET - ECONEA TECHNICAL

Company: 43813 - JANSSEN PHARMACEUTICA INC.

Risk Manager: RM 33 - Marshall Swindell - (703) 308-6341 Room# CM-2 308H

Risk Manager Reviewer: Karen Leavy KLEAVY

Sent Date: 04-May-2005

Calculated Due Date: Oct 31, 2005

Edited Due Date: _____

Type of Registration: Product Registration - Section 3

Action Desc: (A41) NEW AI;NON-FOOD USE;OUTDOOR;OTHER USES;

Ingredients: 119093, 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-(93.2%)

***** Data Package Information *****Expedite: ☐ Yes ☒ No

Date Sent: 06-May-2005

Due Back: _____

DP Ingredient: 119093, 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-

DP Title: _____

CSF Included: ☒ Yes ☐ NoLabel Included: ☒ Yes ☐ No

Parent DP #: _____

Assigned To**Date In****Date Out**

Organization: AD / RASSB

Administrative Due Date: 03-Oct-2005

Team Name: _____

Negotiated Due Date: _____

Reviewer Name: _____

Projected Completion Date: _____

Contractor Name: _____

***** Studies Sent for Review *****

No Studies

***** Additional Data Package for this Decision *****

Printed on Page 2

***** Data Package Instructions *****

Please review the following acute toxicity studies submitted in support of registration of the new chemical ECONEA. Acute oral(MRID No. 456739-20), Acute oral(Fixed Dose Procedure) in rats(MRID No. 456739-15), Acute Dermal Toxicity(LD50) test in Rats(MRID No. 456739-16), Acute Inhalation toxicity study in Rats(MRID No. 4456739-17), Acute Dermal Irritation in Rabbits(MRID No. 456739-18), Buehler Test in Guinea Pigs for Delayed Skin Sensitisation Potential(MRID No. 456739-19), and Primary Eye Irritation Study in Rabbits(MRID No. 465394-00), copy of proposed labeling, and CSF. Action Code A41, PRIA, Attn: Tim McMahon

DATA PACKAGE BEAN SHEET

Date: 04-Feb-2005

Page 1 of 2

***** Registration Information *****

Registration: 43813-ET - ECONEA TECHNICAL

Company: 43813 - JANSSEN PHARMACEUTICA

Risk Manager: RM 33 - Marshall Swindell - (703) 308-6341 Room# CM-2 308H

Risk Manager Reviewer: Karen Leavy KLEAVY

Sent Date: _____

Calculated Due Date: 12-Aug-2007

Edited Due Date: _____

Type of Registration: Product Registration - Section 3

Action Desc: (A41) NEW AI;NON-FOOD USE;OUTDOOR;OTHER USES;

Ingredients: 119093, 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-(93.2%)

***** Data Package Information *****Expedite: ☐ Yes ☒ No

Date Sent: 04-Feb-2005

Due Back: _____

DP Ingredient: 119093, 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-

DP Title: _____

CSF Included: ☒ Yes ☐ NoLabel Included: ☒ Yes ☐ No

Parent DP #: _____

Assigned To**Date In****Date Out**

Organization: AD / RASSB

Administrative Due Date: 23-Aug-2007

Team Name: RASSB1

Negotiated Due Date: _____

viewer Name: _____

Projected Completion Date: _____

Contractor Name: _____

***** Studies Sent for Review *****

No Studies

***** Additional Data Package for this Decision *****

Printed on Page 2

***** Data Package Instructions *****

PLEASE REVIEW THE REBUTTAL LETTER IN RESPONSE TO OUR LETTER OF JUNE 1ST, 2004 CONCERNING ECOLOGICAL EFFECTS REVIEW
ACTION CODE A41, ADMIN DUE DATE 08-12-2007, RASSB DUE DATE 07-12-2007

SUBMISSION BAR CODE #

220066

REVIEWER

RM

5759.391

CODING FORM FOR APPLICATIONS FOR REGISTRATION/AMENDMENTS

FILE SYMBOL/REG NO.

43815-ET

PM

33

ACTION CODE

115

DESCRIPTOR

New Product Labels

☐ CHILD RESISTANT PACKAGING:☐

CERTIFICATION

☐

NON-RESIDENTIAL USE ONLY

☐

NOT APPLICABLE

REGISTRATION TYPE: ☐ CONDITIONAL☐

UNCONDITIONAL

PROPOSED CLASSIFICATION: ☐ GENERAL☐

RESTRICTED USE

DATE ON APPLICATION

EPA RECEIVE DATE

PM RECEIVE DATE

01/09/04

01/21/04

01/23/04

METHOD OF SUPPORT

FORMULATORS EXEMPTION

☐ CITE ALL☐ SELECTIVE☐ NOT SUBMITTED☐ NOT APPLICABLE☐ INCORRECT/RESUB☐ SUBMITTED☐ NOT SUBMITTED☐ NOT APPLICABLE☐ INCORRECT/RESUB

REVIEW(S) REQUESTED

DATA
PACK #DATE
SENTDUE
DATEDATE
RETURNED

CHEMISTRY

EFFICACY

TOXICOLOGY

HED TOX.

ENVIRON. FATE

FISH/WILDLIFE

OTHER

STATUS

Labels can not be processed until the
science reviews are all acceptable

RESPONSE CODE

13

RESPONSE DATE

4/29/04



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

May 21, 2004

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

PLEASE RETURN A COPY OF THIS LETTER WITH PAYMENT

OPP DECISION NUMBER:: D-220066
EPA FILE SYMBOL or REGISTRATION NUMBER: 43813-ET
PRODUCT NAME: ECONEA TECHNICAL
EPA RECEIPT DATE: 12-Mar-2003
EPA COMPANY NUMBER: 43813
COMPANY NAME: JANSSEN PHARMACEUTICA

WILLIAM R GOODWINE
JANSSEN PHARMACEUTICA
PLANT PROTECTION DIVISION
1125 TRENTON-HARBOURTON RD
TITUSVILLE, NJ 08560-0200

SUBJECT: Registration Service Fee Payment Required for New Active Ingredient Application
Not on the Registration Division FY03 Work Plan

Dear Registrant:

The Office of Pesticide Programs has determined that the Action described in the attachment is subject to a Pesticide Registration Service Fee as provided in the Pesticide Registration Improvement Act of 2003 (PRIA). Instructions for submitting payment are also included in the attachment.

Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), section 33 (b)(2)(B)(i) as amended by the PRIA states: "Subject to clause (ii) an application for the registration of a pesticide that was submitted to the Administrator before the effective date of the Pesticide Registration Improvement Act of 2003 and is pending on that effective date shall be subject to a service fee under this section if the application is for a new active ingredient that is not listed on the Registration Division 2003 Work Plan of the Office of Pesticide Programs of the Environmental Protection Agency."

If you believe that you are entitled to a waiver or reduction of the fee as described in the Section 33(b)(7), please submit a copy of this letter and waiver request with the appropriate documentation within 15 days of receipt of this letter to the following address:

By USPS:
Document Processing Desk (FEEWAIV)
Office of Pesticide Programs (7504C)
U.S. Environmental Protection Agency
Ariel Rios Building
1200 Pennsylvania Avenue, NW
Washington, D.C. 20460-0001

By Courier:
Document Processing Desk (FEEWAIV)
Office of Pesticide Programs (7504C)
U.S. Environmental Protection Agency
Room 266A, Crystall Mall 2
1921 Jefferson Davis Highway
Arlington, VA 22202-4501

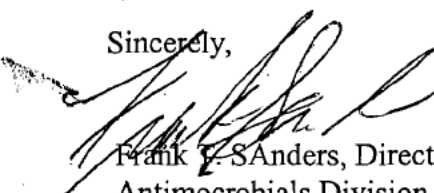
Instructions for submitting a waiver request are attached. Please note that the Agency will not consider a waiver for this action after the 15-day period has expired. If you request a waiver, please do not send payment along with the waiver request.

The net amount due was calculated by determining the fee associated with this action (from the March 17, 2004 Federal register Notice). Any previously submitted tolerance fees were subtracted from this amount. This amount was further reduced in proportion to the amount of work that has been done on the action prior to March 23, 2004.

All Payments must be in United States currency by check, bank draft, or money order drawn to the order of the Environmental Protection Agency. To ensure proper credit, please write the OPP DECISION NUMBER on your check, and enclose a copy of this letter and the attachment with your payment.

We appreciate your cooperation as we begin to implement this new legislation. If you have any questions, please contact Pesticide Registration Service Fee Ombudsman, at (703) 308-6432.

Sincerely,



Frank E. Sanders, Director
Antimicrobials Division

Attachment

PLEASE RETURN A COPY OF THIS LETTER WITH PAYMENT

EPA Company Number: 43813

COMPANY NAME: JANSSEN PHARMACEUTICA

OPP Decision Number: D-220066

EPA File Symbol or Registration Number: 43813-ET

Action for which payment is Required:

Active Ingredient Name: 1H-Pyrrole-3-carbonitrile,4-bromo-2-(4-chlorophenyl)-5-(trifluoromethyl)-

Fee Category: NEW AI;NON-FOOD USE;OUTDOOR;OTHER USES;

Fee Category Amount: \$ 150,000

Less Tolerance Fee Received: \$ 0

Less Discretionary Refund: \$ 67,500

Net Payment Due: \$ 82,500

Please remit payment in the amount of: \$ 82,500 to:

By USPS:

USEPA Washington Finance Center

Pesticide Registration Service Fee

PO Box 360277

Pittsburgh, PA 15251

By Courier:

U.S. EPA Washington Finance Center

Pesticide Registration Service Fee

C/O Mellon Client Service Center

500 Ross Street, Room 670

Box 360277

Pittsburgh, PA 15251-6277

Attn: EPA Module Supervisor

All payments must be in United States currency by check, bank draft, or money order drawn to the order of the Environment Protection Agency. To ensure proper credit, please write the OPP DECISION NUMBER on your check, and enclose a copy of this attachment with your payment.

DECISION PKG. NO. D220066

SUBM. DUE DATE _____

SUBMISSION BAR CODE # 741978REVIEWER KL~~765679~~ 765679**CODING FORM FOR APPLICATIONS FOR REGISTRATION/AMENDMENTS**FILE SYMBOL/REG NO. 43813-ET PM 33 ACTION CODE 115DESCRIPTOR _____ **FQPA** **NFQPA**☐ CHILD RESISTANT PACKAGING: ☐ REQUIRED ☐ NOT REQUIREDREGISTRATION TYPE: ☐ CONDITIONAL ☐ UNCONDITIONAL ☐ RESTRICTED USE

DATE ON APPLICATION

EPA RECEIVE DATE

PM RECEIVE DATE

6, 2, 036, 4, 036, 4, 03

METHOD OF SUPPORT

FORMULATORS EXEMPTION

☐ CITE-ALL ☐ SELECTIVE
☐ NOT SUBMITTED ☐ N/A☐ SUBMITTED ☐ NOT SUBMITTED
☐ N/A

REVIEW(S) REQUESTED

DATA
PACK #DATE
SENTDUE
DATEDATE
RETURNED

CHEMISTRY _____] [_____] [_____] [_____]

EFFICACY _____] [_____] [_____] [_____]

ACUTE TOX. _____] [_____] [_____] [_____]

RASSB TOX. _____] [_____] [_____] [_____]

ENVIRON. FATE _____] [_____] [_____] [_____]

FISH/WILDLIFE _____] [_____] [_____] [_____]

OTHER: _____ : _____] [_____] [_____] [_____]

STATUS _____

RESPONSE CODE

38

RESPONSE DATE

6/1/04

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

JUN 01 2004

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Mr. William Goodwine
Senior Director of the Plant & Material Protection Division for,
Janssen Pharmaceutica, Inc.
11215 Trenton- Harbourton Road
Titusville, NJ 08560

Subject: ECONEA TM Technical
EPA File Symbol 43813-ET
Your Application Dated June 2nd, 2003
EPA Received Date June 4th, 2003

The application referred to above, submitted in connection with registration under the Federal Insecticide, Fungicide, and Rodenticide Act(FIFRA), as amended, is incomplete.

Upon conducting a review of the submitted studies, the following comments apply:

Adsorption/Desorption of the Hydrolysis Products Study for ECONEA:

This study is classified as acceptable and satisfies the guideline requirement for an adsorption/desorption study in sediments.

Adsorption/Desorption Study for ECONEA:

This study is classified as acceptable and satisfies the guideline requirement for adsorption/desorption study in sediment.

Anaerobic Degradation Study for ECONEA:

This study is classified as acceptable and satisfies the guideline requirement for anaerobic degradation study in two water sediment systems.

Hydrolysis Data for ECONEA:

This Hydrolysis study satisfies the data requirements and the findings/conclusions are scientifically sound.

Aerobic Degradation Study for ECONEA:

This study is classified as acceptable and satisfies the guideline requirement for aerobic bio-transformation study in two water-sediment systems.

Thank you for your submission of revised product labeling. It will be used during review of your application.

				CONCURRENCES			
SYMBOL							
SURNAME							
DATE							

The product mentioned above has not passed the chemical screen; however, based upon our agreement to initiate a review of all submitted data, except toxicity data due to missing studies, data reviews are still being processed.

As per our letter of March 18th, 2003, due to the unusual circumstances associated with this new active ingredient, the Agency is still reviewing the ecological effects data and end-use application into review in the absence of a complete data package. Normally, a new active ingredient submission must be complete package before the Agency will start its review process.

Please note that when toxicology data are submitted they will be placed into review on a track independent of the environmental and other reviews.

The product may not be lawfully distributed in interstate commerce until the above discrepancies have been clarified.

If you have any questions concerning this letter, please contact Karen M. Leavy-Munk at (703)-308-6237.

Sincerely,



Marshall Swindell
Product Manager 33
Regulatory Management Branch I
Antimicrobial Division(7510C)



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

JUN -1 2004

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Mr. William Goodwine
Senior Director of the Plant & Material Protection Division for,
Janssen Pharmaceutica, Inc.
11215 Trenton-Harbourton Road
Titusville, NJ 08560

Subject: ECONEA TM Technical
EPA File Symbol 43813-ET
Your Application Dated June 2nd, 2003
Submission Dated June 4th, 2003

The application referred to above, submitted in connection with registration under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended, is incomplete.

Upon conducting a review of the submitted studies, the following comments apply:

The Agency has reviewed the ecotoxicity studies submitted in support of Chlorfenapyr (ECONEA) registration as an antifoulant paint. Aquatic animal, plant, and whole sediment toxicity tests were submitted for the active ingredient R107894, the first primary degradate CL322,250, and two additional degradates CL322,248 and CL 325,195.

The following studies have been reviewed and a brief summary is presented. For further details, please refer to enclosed DERs.

1. The study entitled, "Acute toxicity of R107894 technical for fish, *Lepomis machronchirus* {MRID No. 456740-02}, Guideline No. 850.1075, is invalid and not repairable. The study needs to be repeated.

The rationale for the classification of invalid is due to an apparent cross-contamination of the solvent control with the test chemical.

Refer to the DER for further information.

2. The study entitled, "Acute toxicity of R107894 technical for fish, *Oncorhynchus mykiss* {MRID No. 456740-01}, Guideline No. 850.1075, is classified as invalid and not repairable. The study needs to be repeated.

The rationale of the classification of invalid is due to the concerns regarding whether dechlorinated water was used, as well as failure of the measured concentrations of the test chemical to remain above 80% of the nominal. Measured concentrations were frequently below the limit of detection, causing uncertainty regarding the actual levels of test chemical to which organisms were exposed. No explanation or justification was given for the loss of test chemical during the study. Finally, no pre-test culture conditions were provided (e.g., mortality, signs of disease).

Refer to the DER for further information.

3. The study entitled, "Acute toxicity of R107894 technical for *Daphnia magna* {MRID No. 456740-04}", Guideline No. 850.1010, is classified as invalid and not repairable. The study needs to be repeated.

The rationale for the classification of invalid is due to an unexplained loss of chemical during the test, so much so, that measured concentrations were below the limit of detection, making it impossible to determine what the actual levels were to which the organisms were exposed. Additionally, information on pre-test condition of the daphnid culture was not provided, (e.g., disease/mortality, presence of ephippia, etc). If ephippia are present, test is invalid.

Refer to the DER for further information.

4. The study entitled, "Acute Toxicity of R107894 Technical for *Daphnia magna* {MRID No. 457069-01}", Guideline No. 850.1010, is classified as invalid and repairable. The study needs to be repeated.

The test must be repeated with more frequent test chemical verification and additional measures to maintain test chemical levels in the treatment vessels.

The rationale for the classification of invalid is due to the test concentration not being adequately maintained during the test; actual levels to which organisms were exposed could not be determined.

The test must be repeated with more frequent test chemical verification and additional measures to maintain test chemical levels in the treatment vessels.

Refer to the DER for further information.

5. The study entitled, "*Daphnia magna* Reproduction Test of R107894 Technical {MRID No. 456740-08}", Guideline No. 850.1300, is classified as invalid and not repairable. The study needs to be repeated.

The rationale of the classification of invalid is due to the control daphnids failed to produce an average of >60 young; details of test organisms prior to test initiation (e.g., presence of ephippia, mortality, production of young, etc.) were not provided, DO levels dropped as low as 39% during the test (must remain >60%).

Refer to the DER for further information.

6. The study entitled, R107894-Acute toxicity to Sheepshead Minnow(*Cyprinodon variegatus*) Under Flow-Through Conditions {MRID No. 456740-03}, Guideline No.850.1075, is classified as supplemental and not repairable. The study does not need to be repeated.

The rationale of the classification of invalid due to the test chemical concentrations were not measured according to Guideline recommendations. This results in uncertainty regarding the actual levels to which the organisms were exposed throughout the test.

Refer to the DER for further information.

7. The study entitled, R107894-Acute toxicity to Eastern Oysters(*Crassostrea virginica*) Under Flow-Through Conditions {MRID No. 456740-05}, Guideline No.850.1025, is classified as supplemental and not repairable. The study does not need to be repeated.

The rationale of the classification of supplemental is due to the lack of a NOEC level. A NOEC was not achieved; shell deposition at the lowest level tested was significantly reduced compared to controls(23% inhibition).

Refer to the DER for further information.

8. The study entitled, R107894-Life-Cycle Toxicity Test with Mysids(*Americamysis bahia*), {MIRD No. 456740-09}, Guideline No. 850.1350456740-09, is classified as supplemental and not repairable. The study does not need to be repeated.

The rationale of the classification of supplemental is due to no growth endpoint determined, body weights/lengths only reported at test termination.

Refer to the DER for further information.

9. The study entitled, Alga, Growth Inhibition Test-Effect of R107894 Technical on the Growth of *Raphidocelis subcapitata*, {MRID No. 456741-17}, Guideline No. 850.5400, is classified as supplemental and not repairable. The study needs to be repeated.

The rationale of the classification of supplemental is due to lighting being too intense(range from 7,500 to 12,500 lux) , and variable(replicates B and C averaged 8,500 lux, Replicate A averaged 12, 500 lux)-may have affected results. Guideline recommends 4,300 lux applied over all replicates.

Refer to the DER for further information.

10. The study entitled, Alga, Growth Inhibition Test Effect of R107894 Technical on the Growth of *Skeletonema costatum*, {MRID No. 456741-18}, Guideline No. 850.5400 (Tiers I and II), is classified as supplemental and not repairable. The study needs to be repeated.

The rationale of the classification of supplemental is due to the loss of replicate at 8.62 ug/L dosage was not explained. Light intensity too high, photo-period missing (14 hrs. light, 10 hrs. dark required), oscillation rate may have been too high (maximum speed of 60 cycles/minute required), initial cell concentration too low (10K cells vs 77K cells required).

Refer to the DER for further information.

11. The study entitled, Acute toxicity of CL 322, 250 for fish, *Lepomis macrochirus*, {MRID No. 456740-23}, Guideline No. 850.1075, is classified as invalid and not repairable. The study needs to be repeated.

The rationale of the classification of invalid is due to the use of dechlorinated water. Use of dechlorinated water requires that daily chlorine residues be measured during the study and results provided with the study report, or additional testing to demonstrate that the dechlorinated water can support aquatic life must be submitted. The test chemical was detected at 7.02 ppb in one control replicate during the study; while this apparently did not cause any mortalities to the control fish; it indicates poor laboratory methodology, which could impact study results. Additionally, measured concentrations were < 80% of nominal. In several replicate chambers, and no information on pretest fish conditions (e.g., disease, mortalities, age/population information) were provided in the report. Additionally, test was conducted at levels up to 2.98 mg/L, but the LC₅₀ level was not achieved. Guidelines require that treatment levels be high enough to achieve the LC₅₀ level or reach 100 mg/L.

Refer to the DER for further information.

12. The study entitled, Acute toxicity of CL 322, 250 for fish, *Oncorhynchus mykiss*, {MRID No. 456740-22}, Guideline No. 850.1075, is classified as invalid and not repairable. The study needs to be repeated.

The rationale for the classification of invalid is due to the report stating that "tap water" was used as dilution water; no indication was made as to whether or not this was dechlorinated. If dechlorinated water is used, testing of residue chlorine levels must be included in the report and/ or separate testing results showing the water can support aquatic life must be included. Additionally, no information on the condition of the culture pre-test was provided (e.g., mortality, disease treatment, etc.) and the measured concentrations dropped to as low as 54.2% of nominal, without explanation/ justification.

Refer to the DER for further information.

13. The study entitled, Acute toxicity of CL322,250 for *Daphnia magna*, {MRID No. 456741-02}, Guideline No. 850.1010, is classified as supplemental and repairable. The study can be upgraded if the additional information in the DER is provided to the Agency for our review. The study needs to be repeated.

The rationale for the classification of supplemental is due to a need for more information on culture condition(e.g., pretest mortality, presence of ephippia, etc.).

Refer to the DER for further information.

14. The study entitled, Acute toxicity of CL 322,250 for *Daphnia magna*, {MRID No. 456069-03}, Guideline No. 850.1010, is classified as supplemental and repairable. The study can be upgraded if the information /justification of low chemical recovery is provided. The study needs to be repeated.

The rationale for the classification of supplemental is due to the recovery of test chemical(mean measured vs nominal) was 29-32%, which is well below the Guideline requirement of 85- 115%. This was not explained/justified in the study report. Laboratory stability tests for the chemical in the test medium showed greater recoveries, but do not report time period. Other Major deficiencies include lack of information on acclimation and culture condition(e.g., pre-test mortality, presence of ephippia, etc.), and lack of description on methods by which organisms were added to test vessels(e.g., random and impartial methods).

Refer to the DER for further information.

15. The study entitled, Fish Early Life-Stage Toxicity Test of CL322,250, {MRID No. 456741-05}, Guideline No. 850.1400, is classified as invalid and not repairable. The study needs to be repeated.

The rationale for the classification of invalid is due to the "tap water" being used as the basis for the demineralized water used as dilution water; it is not stated if the water is de-chlorinated. Use of dechlorinated water requires daily testing of chlorine residues during the study, or testing to demonstrate that the water can support aquatic life. Additionally, the laboratory could not verify that organophosphorous concentrations in the Instant Ocean mix used were below EPA Guideline requirements, as the limit of detection used in analysis was greater than the allowable limit.

Refer to the DER for further information.

16. The study entitled, *Daphnia magna* reproduction test of CL 322,250, {MRID No. 456741-07}, Guideline No. 850.1075, is classified as invalid and not repairable. The study needs to be repeated.

The rationale for the classification of invalid is due to the source of dilution water being unknown; if dechlorinated tap water, daily testing of chlorine residues or testing to demonstrate water can support aquatic life must be submitted. Additionally, no information on pretest culture condition (e.g., disease, mortality, presence of ephippia) were reported; presence of ephippia invalidates a study. The range of concentrations selected for this study were inappropriate because 100% mortality occurred in the highest test concentration and the data for the other test concentrations were not statistically different from the control data. Therefore, LOEC, MATC, and EC₅₀ values for the number of offspring and the length of parents could not be calculated and NOEC values could only be reported as greater than the highest test concentrations.

Refer to the DER for further information.

17. The study entitled, CL 322,250-Acute toxicity to Sheepshead Minnow (*Cyprinodon variegatus*) Under Flow-Through Conditions, {MRID No. 456741-01}, Guideline No. 850.1075, is classified as supplemental and not repairable. The study needs to be repeated.

The rationale of the classification of supplemental is due to the lack of a LD₅₀ level. The testing conducted at high enough levels for the non-specific endpoint (LD50.0.95 mg/L) to be adequate for risk assessment. Laboratory tests for recovery with this substance in the same medium used in this test (Hoaglund's medium) used levels as high as 2.0 mg/L, which is twice the "functional solubility level" of 1.0 mg/L reported in this study. Use of other solvents or additional methodology should be employed to allow testing at higher levels (see OPPTS Guidance Document 850.1000 for more information). Additional Guideline deviations of concern in this study are:

1. The Guideline states that the test substance should be measured in each replicate at 0, 48, and 96 hours. In the Study Report, concentrations were not reported for each replicate (a mean value was reported for each set of replicates) and were only measured at the start (0 hours) and end of test (96 hours);
2. No details were provided on when the fish were added to the test chambers, in relation to the addition of the test substance. Also, the Study Report does not indicate if any disease treatment was administered to the fish 48 hours prior to test initiation or during the test; and
3. Information pertaining to the acclimation of the fish (disease treatment, pretest mortality, water temperature) was not provided.

18. The study entitled, Alga, Growth Inhibition Test Effects of CL322, 250 on the Growth of *Raphidocelis subcapitata*, {MRID No. 456741-23}, Guideline No. 850.5400, is classified as supplemental and repairable. The study does not need to be upgraded.

The rationale of the classification of supplemental is due to the basis for the 2.20 mg/L outlier was not provided; oscillation rate of "maximum speed" must be defined. A high oscillation rate could facilitate the loss of test chemical from the test flasks.

Refer to the DER for further information.

19. The study entitled, CL 322,250-Toxicity to the Freshwater Blue-Green Alga, *Anabaena flos-aquae*, {MRID No. 458939-07}, Guideline No. 850.5400, is classified as supplemental and not repairable. The study does not need to be repeated.

The rationale of the classification of supplemental is due to a lack of an EC_{50} level. On page 10 of the study report, it states: "Additional testing to further define the EC_{50} values was not performed because the highest measured concentration exceeded the EC_{50} (96 hour cell density EC_{50} = 0.35 mg a.i./L) for the parent compound, R107894." CL 322,250 testing should remain independent of R107894 test results. An EC_{50} value was not determined.

Refer to the DER for further information.

20. The study entitled, CL 325,250-Toxicity to the Freshwater Diatom, *Navicula pelliculosa*, {MRID No. 458939-08}, Guideline No. 850.5400, is classified as supplemental and not repairable. The study does not need to be repeated.

The rationale of the classification of supplemental is due to the dosages did not produce an EC_{50} value. An EC_{50} value is needed for risk assessment purposes.

Refer to the DER for further information.

21. The study entitled, Alga, Growth Inhibition Test Effect of CL322, 250 on the Growth of *Skeletonema costatum*, {MRID No. 456741-24}, Guideline No. 850.5400, is classified as supplemental and not repairable. The study needs to be repeated.

The rationale of the classification of supplemental is due to the loss of replicate at 1.41 mg ai/L dosage not explained, light intensity too high, photoperiod missing (14 hours light, 10 hours dark is required), oscillation rate may have been too high (maximum speed?), initial cell concentration too low, see other deviations below. NOEC was not determined, however, the approximate EC_{50} value of 0.18 mg ai/L, based on % growth inhibition-Table 4, pg. 21 of 23 is useful in lieu of the NOEC.

Refer to the DER for further information.

22. The study entitled, CL 322,250-Toxicity to Duckweed, *Lemna gibba*, {MRID No. 456741-22}, Guideline No. 850.4400, is classified as supplemental and not repairable. The study does not need to be repeated.

The rationale of the classification of supplemental is due to the treatment levels not bracketing the EC_{50} value for frond density or growth rate.

Refer to the DER for further information.

23. The study entitled, Acute toxicity of Chlorfenapyr Soil Metabolites to the Bluegill Sunfish, *Lepomis macrochirus*, Under Static Test Conditions for CL 303267 and CL 325195, {MRID No. 444526-17}, Guideline No. 72-1, is classified as invalid but repairable. The study does not need to be repeated.

The rationale of the classification of invalid is due to these studies not meeting the guideline requirements for acute toxicity tests using bluegill sunfish. Guideline require that concentrations be measured at the beginning and end of the test. At the conclusion of both of these tests, concentrations were not measured at any test level. Further, chemical analysis was not performed. Although these tests were static tests, a rationale for the lack of a chemical analysis should be generated, and submitted to the Agency for our review. Chemical characteristics such as solubility and absorbing tendencies of this compound would be useful. Until such rationale can be provided, these studies must be classified as invalid. However, upon submission of this rationale, these studies could be upgraded to supplemental or core status.

Refer to the DER for further information.

24. The study entitled, Acute toxicity of Chlorfenapyr Soil Metabolites to *Daphnia magna* Under Static Test Conditions for CL312094, CL 325195, CL 303267, {MRID No. 444526-18}, Guideline No. 72-2, is classified as invalid. The study does not need to be repeated.

The rationale of the classification of invalid is due to these studies not meeting the guideline requirements for an acute freshwater invertebrate toxicity test. Guideline require that concentrations be measured at the beginning and end of the test. At the conclusion of these tests, concentrations were not measured at any test level. Further, chemical analysis was not performed. Although these tests were static tests, a rationale for the lack of a chemical analysis needs to be generated and submitted to the Agency for our review. Chemical characteristics such as solubility and adsorbing tendencies of this compound would be useful. Until such rationale can be provided, these studies must be classified as invalid. However, upon submission of this rationale, these studies could be upgraded to supplemental or core status.

Refer to the DER for further information.

25. The study entitled, Acute toxicity of CL 325, 195 for *Daphnia magna*, {MRID No. 457069-02}, Guideline No. 850.1010, is classified as supplemental and repairable. The study may be upgraded if missing information is provided. The study does not need to be repeated.

The rationale of the classification of invalid is due to the lack of reported information acclimation, pre-test condition of culture(e.g., morality, presence of ephippia), and methods used to add organisms to test vessels(e.g., random and impartial methods).

Refer to the DER for further information.

26. The study entitled, Fish Early Life-Stage Toxicity Test of CL 325, 195, {MRID No. 456740-16}, Guideline No. 850.1400, is classified as invalid and not repairable. The study does not need to be repeated.

The rationale of the classification of invalid is due to "tap water" being used as the basis for the demineralized water used as dilution water; it is not stated if the water was dechlorinated. Use of dechlorinated water requires daily test of chlorine residues during the study, or testing of chlorine residue during study, or testing to demonstrate that the water can support aquatic life. Additionally, the laboratory could not verify that organophosphorous concentrations in the Instant Ocean mix were used were below the EPA Guideline requirements, as the limit of detection used in the analysis was greater than the allowable limit.

Refer to the DER for further information.

27. The study entitled, *Daphnia magna* Reproduction Test of CL 325, 195, {MRID No. 456740-18}, Guideline No. 850.1300, is classified as invalid and repairable. The study may be upgraded to supplemental, if pre-test data verifying the lack of ephippia and other culture conditions is submitted. The study does not need to be repeated.

The rationale of the classification of invalid is due to the lack of pre-test culture information (e.g., mortality, disease, presence of ephippia); presence of ephippia invalidates a study. Other significant deviations include an unacceptable range of concentrations used-100% mortality at highest level tested, no statistically significant effects on growth or reproduction at the next lower level, which precludes achieving any useful reproduction or growth effect endpoints to use in a risk assessment.

Refer to the DER for further information.

28. The study entitled, CL325, 195-Acute Toxicity to Sheepshead Minnow (*Cyprinodon variegatus*), {MRID No. 456740-13}, Under Flow-Through Conditions, is classified as supplemental and not repairable. The study does not need to be repeated:

The rationale for the classification of invalid is due to the measured concentrations only taken at test initiation and termination-no way to determine variability of concentration during the 96-hour study, and therefore there is uncertainty about the actual exposure exposure levels throughout the test.

Refer to the DER for further information.

29. The study entitled, CL 325, 195-Toxicity to Amphipods(*Hyalella azteca*) During a 10-Day Sediment Exposure, {MRID No. 456740-19}, Guideline No. 850.1735, is classified as supplemental and not repairable. The study does not need to be repeated.

The rationale of the classification of invalid is due to the organic solvent added to the test but did not appear to adversely affect the test species, no data analysis of sediment.

Refer to the DER for further information.

30. The study entitled, Alga, Growth Inhibition Test Effect of CL 325,195 on the Growth of *Raphidocelis subcapitata*, {MRID No. 456741-20}, Guideline No. 850.5400 (Tiers I and II), is classified as supplemental and repairable. The study can be upgraded to core if the EC_{05} of 0.23 mg ai/L is acceptable in lieu of NOEC. The study does not need to be repeated.

The rationale of the classification of invalid is due to the lack of determining a NOEC level.

Refer to the DER for further information.

31. The study entitled, Alga, Growth Inhibition Test Effects of CL 325, 195 on the Growth of *Skeletonema costatum*, {MRID No. 456741-21}, Guideline No. 850.5400(Tiers I and II), is classified as supplemental and not repairable.

The rationale of the classification of invalid is due to the light intensity too high, photoperiod missing(14 hrs. light, 10 hrs. dark is required), oscillation rate may have been too high (maximum speed of 60 cycles/minute required), initial cell concentration too low(10K cells vs 77K cells required).

Refer to the DER for further information.

32. The study entitled, Acute toxicity of CL 322,248 for fish, *Lepomis macrochirus*, {MRID No. 456741-11, Guideline No. 850.1075, is classified as invalid and not repairable. The study does not need to be repeated.

The rationale of the classification of invalid is due to the use of dechlorinated water instead of dilution water. Use of dechlorinated water requires daily chlorine analysis or testing to demonstrate that the water can be used to support aquatic life. Additional deviations, such as the unexplained loss of test chemical and higher than allowable variation between replicate vessels, also compromise the scientific validity of this study. Additionally, the study tested only one concentration, 4.42 mg/L. When such a limit test is performed, it must be at a level ≥ 100 mg/L to be acceptable for fulfillment of Guideline 72-1/850.1075 requirements, unless justified(e.g., solubility issues).

Refer to the DER for further information.

33. The study entitled, Acute toxicity of CL 322,248 for fish, *Oncorhynchus mykiss*, {MRID No. 456741-10}, Guideline No. 850.1075, is classified as invalid and repairable. The study may be upgraded to supplemental, if information provided to indicate dilution water was not dechlorinated tap water. The study does not need to be repeated.

The rationale of the classification of invalid is due to the study report not stating if the "tap water" being used is dechlorinated; use of dechlorinated water requires daily sampling of chlorine residues or separate testing to demonstrate water supports aquatic life. Additionally, test was only conducted at 2.71 mg/L, as a limit test; for limit testing to be acceptable for Guideline fulfillment, concentration tested must be ≥ 100 mg/L, unless justified(e.g., solubility issues with no solvents or methods successfully increasing solubility to 100mg/L). Also, no information on pre-test fish conditions(e.g. disease, mortality) was provided, nor was information on how/when fish were added to treatment vessels provided.

Refer to the DER for further information.

34. The study entitled, Acute toxicity of CL 322,248 for *Daphna magna*, {MRID No. 456741-12}, Guideline No. 850.1010, is classified as supplemental and not repairable. The study needs to be repeated. The study does not need to be repeated.

The rationale of the classification of invalid is due to the very low recovery of chemical (23-25%) with no explanation/justification; lack of information on acclimation period and culture condition(e.g., pretest mortality, presence of ehippia, etc.); lack of information on how organisms were added to test vessels(e.g., random and impartial methods); final sampling for test chemical concentration only performed in one replicate of each treatment level.

Refer to the DER for further information.

35. The study entitled, *Daphna magna* Reproduction Test of CL 322,248, {MRID No. 456741-13}, Guideline No. 850.1300, is classified as supplemental and not repairable. The study does not need to be repeated.

The rationale of the classification of invalid is due to the various deviations for Guideline requirements, most noticeably: no NOEC achieved for the most sensitive endpoint in this test, length of adult daphnids at test termination; lack of information on the conditions of the test organisms prior to the start of the test period. Therefore, it is not known if the cultures contained ephippia, if adults in the cultures did not produce young before day 12, if more than 20% of the culture shock died in the two days before the test, if adults in the culture did not produce an average of at least 3 young per day over previous test. (According to the OPPTS Guideline, daphnids should not be used in the test if they meet any of these conditions); measured concentrations were only taken in half of the replicates at each concentration level; low recovery of the test material(51-52%) with no explanation.

Refer to the DER for further information.

36. The study entitled, CL 322,248- Toxicity to Amphipods(*Hyalella azteca*) During a 10-Day Sediment Exposure, {MRID No. 456958-04}, Guideline No. 850.1735, is classified as invalid. The study does not need to be repeated.

The rationale of the classification of invalid is due to the poor recovery of test chemical indicative of some larger problem with this test. Numerous guideline deviations occurred (see below) most notable of which were DO % saturation not reported, description of sediment not given, solvent used, dry weights not given or discussed in the Study Report.

Refer to the DER for further information.

37. The study entitled, Alga, Growth Inhibition Test Effect of CL 322-248 on the Growth of *Raphidocelis subcapitata*, {MRID No. 456741-26}, Guideline No. 850.5400 (Tiers I and II), is classified as supplemental and not repairable. The study does not need to be repeated.

The rationale of the classification of supplemental is due to the EC_{50} not being achieved, basis for outlier at 1.99 mg ai/L dosage not provided, "maximum speed" of oscillator not defined, reasons for not achieving logarithmic growth at dosages having stimulatory effects on algal growth not understood by study authors.

Refer to the DER for further information.

38. The study entitled, CL 322,248-Toxicity to the Freshwater Blue-Green Alga, *Anabaena flos-aquae*, {MRID No. 458939-04}, Guideline No. 850.5400, is classified as supplemental and not repairable. This study does not need to be repeated.

The rationale of the classification of supplemental is due to a EC_{50} value was not obtained. The test needs to be conducted at higher dosages.

Refer to the DER for further information.

39. The study entitled, CL 322,248-Toxicity to the Freshwater Diatom *Navicula pelliculosa*, {MRID No. 458939-05, Guideline No. 850.5400 (Tiers I and II), is classified as supplemental and not repairable. The study does not need to be repeated.

The rationale of the classification of supplemental is due to not obtaining an EC_{50} value.

The test needs to be conducted at higher dosages.

Refer to the DER for further information.

40. The study entitled, Alga, Growth Inhibition Test Effect of CL 322,248 on the Growth of *Skeletonema costatum*, {MRID No. 456741-27}, Guideline No. 850.5400, is classified as supplemental and not repairable. The study does not need to be repeated.

The rationale of the classification of supplemental is due to the light intensity being too intense; no photoperiod used as required; maximum oscillation speed not described; optimum logarithmic growth not achieved; >90% inhibition at higher dosage not achieved.

Refer to the DER for further information.

41. The study entitled, CL 322,248- Toxicity to Duckweed, *Lemna gibba*, {MRID No. 456741-25}, Guideline No. 850.4400, is classified as supplemental and not repairable. The study does not need to be repeated.

The rationale of the classification of supplemental is due to the study's failure to determine an EC_{50} value.

Refer to the DER for further information.

The following studies are classified as core and acceptable.

1. The study entitled, 14-Day Acute Toxicity Test with AC 303,268 Technical in Northern Bobwhites (*Collinus virginiana*), {MRID No. 434928-09}, Guideline No. 71-1(A), is classified as core.
2. The study entitled, Avian Single-Dose LD50 Test, {MRID No. 434928-08}, Guideline No. 71-1(A), is classified as core.
3. The study entitled, R107894-Early Life-Stage toxicity with Zebra Fish (*Danio rerio*), {MRID No. 458939-01}, Guideline No. 850.1400, is classified as core.
4. The study entitled, R107894-Acute Toxicity to Mysids (*Americamysis bahia*) Under Flow -Through Conditions, {MRID No. 456740-06}, Guideline No. 850.1035, is classified as core.
5. The study entitled, R107894-Early Life Stage Toxicity Test with Sheepshead Minnow (*Cyprinodon variegatus*), {MRID No. 456740-07}, Guideline No. 850.1400, is classified as core.
6. The study entitled, R107894-Toxicity to Amphipods (*Hyalella azteca*) During a 10-Day Sediment Exposure, {MRID No. 456740-10}, Guideline No. 850.1735, is classified as core.
7. The study entitled, R107894-Toxicity to Marine Amphipods (*Leptocheirus plumulosus*) During 10-Day Sediment Exposure, {MRID No. 456740-11}, Guideline No. 850.1740, is classified as core.
8. The study entitled, R107894-Toxicity to the Freshwater Blue-Green Alga, *Anabaena flos-aquae*, {MRID No. 458939-02}, Guideline No. 850.5400, is classified as core.
9. The study entitled, R107894-Toxicity to the Freshwater Diatom, *Navicula pelliculosa*, {MRID No. 458939-03}, Guideline No. 850.5400 (Tiers I and II), is classified as core.
10. The study entitled, R107894-Determination of Effects on Seedling Emergence of Rice (*Oryza sativa*), {MRID No. 456741-15}, Guideline No. 850.4100, is classified as core.
11. The study entitled, R107894-Toxicity to Duckweed, *Lemna gibba*, {MRID No. 456741-16}, Guideline No. 850.440, is classified as core.
12. The study entitled, CL 322,250-Acute Toxicity to Eastern Oysters (*Crassostrea virginica*) Under Flow Through Conditions, {MRID No. 456741-03}, Guideline No. 850.1025, is classified as core.

13. The study entitled, CL 322,250-Acute Toxicity to Mysids(*Americamysis bahia*) Under-Flow Through Conditions, {MRID No. 456741-04}, Guideline No. 850.1035, is classified as core.
14. The study entitled, CL 322,250-Early Life -Stage Toxicity Test with Sheepshead Minnow(*Cyprinodon variegatus*), {MRID No. 456741-06, Guideline No. 850.1400, is classified as core.
15. The study entitled, CL 322,250-Toxicity to Amphipods(*Hyalella azteca*) During 10-Day Sediment Exposure,{MRID No. 456741-08}, Guideline No. 850.1735, is classified as core.
16. The study entitled, CL 322,250-Toxicity to Marine Amphipods (*Leptocheirus plumulosus*) During a 10-Day Sediment Exposure, {MRID No. 456741-09}, Guideline No. 850.1740, is classified as core.
17. The study entitled, Avian Single-Dose Oral LD50 Test with CL325,195 in Northern Bobwhite(*Colinus virginianus*), {MRID No. 444526-11}, Guideline No. 71-1(A), is classified as core.
18. The study entitled, Avian Single-Dose Oral LD50 Test with CL325,195 in Mallard Duck(*Anas platyrhynchos*), {MRID No. 444526-12}, Guideline No. 71-1(A), is classified as core.
19. The study entitled, CL322,195-Acute Toxicity to Eastern Oysters(*Crassostrea virginica*) Under Flow -Through Conditions, {MRID No. 456740-14, Under Flow-Through Conditions, {MRID No. 456740-14}, Guideline No. 850.1025, is classified as core.
20. The study entitled, CL 325,195-Acute Toxicity to Mysids (*Americamysis bahia*) Under Flow-Through Conditions, {MRID No. 456740-15}, Guideline No. 850.1035, is classified as core.
21. The study entitled, CL 325, 195-Early Life Stage Toxicity Test with Sheepshead Minnow (*Cyprinodon variegatus*), {MRID No. 456740-17}, Guideline No. 850.1400, is classified as core.
22. The study entitled, CL 235, 195-Toxicity to Marine Amphipods (*Leptocheirus plumulosus*) During a 10-Day Sediment Exposure, {MRID No. 456740-20}, Guideline No. 850.1740, is classified as core.
23. The study entitled, CL 325,195-Toxicity to the Freshwater Blue-Green Alga, *Anabaena flos-aquae*, {MRID No. 459452-01}, Guideline No. 850.5400, is classified as core.
24. The study entitled, CL325,195-Toxicity to the Freshwater Diatom, *Navicula pelliculosa*, {MRID No. 456741-06}, Guideline No. 850.4400, is classified as core.
25. The study entitled, CL325,195-Toxicity to Duckweed *Lemna gibba*,{MRID No. 456741-19}, Guideline No. 850.4400, is classified as core.

26. The study entitled, CL322,248-Toxicity to Marine Amphipods(*Leptocheirus plumulosus*) During a 10-Day Sediment Exposure, {MRID No. 456741-14}, Guideline No. 850.1740, is classified as core.

The following tables list the outstanding ecotoxicity studies. It has been determined that due to rapid degradation of R107894 to CL 322, 250 many of the acute and chronic toxicity tests must be repeated(invalid or supplemental ratings). Fish and oysters BCFs are also required for these chemicals. The CL322,248 degradate, which is debrominated form of CL322,250 found under anaerobic conditions and in saltwater is a toxicity concern as well.

Econea-Outstanding Eco Effects Data

Econea Technical (aka R107894, AC303,268)

Study	Species	Status
Avian dietary-850.2200	bobwhite	Reserved
Avian dietary-850.220	mallard	Required
FW-fish acute-850.1075	bluegill	Required(repeat of submitted study)
FW fish acute-850.1075	trout	Required(repeat of submitted study)
FW invert acute-850.1010	daphnid	Required(repeat of submitted study)
FW invert life cycle-850.1300	daphnid	Required(repeat of submitted study)
Fish BCF-850.1730	bluegill	Required
Oyster BCF-850.1710	E.Oysters	Required
GreenAlgae-850.5400	<i>Selenastrum capricornutum</i>	Required(repeat of submitted study)
Marine diatom-850.5400	<i>Skeletonema costatum</i>	Required(repeat of submitted study)

Major Degradate, CL 322,250

Study	Species	Status
Avian acute oral-850.2100	mallard	Required
Avian dietary-850.2200	bobwhite	Reserved
FW fish acute-850.2200	mallard	Required
FW fish acute-850.1075	bluegill	Required(repeat of submitted study)
FW fish acute-850.1075	trout	Required(repeat of submitted study)
FW fish invert acute-850.1010	daphnid	Required(repeat of submitted study)
FW fish ELS-850.1400	zebra fish	Required(repeat of submitted study)
FW invert life cycle-850.1300	daphnid	Required(repeat of submitted study)
ME fish acute-850.1075	sheepshead	Required(repeat of submitted study)
ME invert lifecycle-850.1350	mysid	Required
Fish BCF-850.1730	bluegill	Required
Oyster BCF-850.1710	E. Oyster	Required
Marine Diatom-850.5400	Skeletonema costatum	Required(repeat of submitted study)

Degradate, CI 322, 248 (de-brominated CL322,250-found in saltwater and anaerobic conditions)

Study	Species	MRID
Avian acute oral-850.2100	mallard	Required
Avian dietary-850.2200	bobwhite	Required
Avian dietary-850.220	mallard	Required
ME fish acute-850.1075	sheepshead	Required
ME mollusk acute-850.1025	E.oyster	Required
ME invert acute-850.1035	mysid	Required
ME fish ELS-850.1075	Sheepshead	Required
ME invert lifecycle-850.1350	mysid	Required

Further, bromine released during the degradation process must be characterized. A significant amount of bromine could be toxic to aquatic plants and animals and may necessitate ecotoxicity testing for risk assessment.

Resubmit all the studies listed as "required" and/or "repeat of submitted study" to Agency for our review and to satisfy the ecotoxicity guideline requirements.

Refer to the provided copy of the Agency memorandum regarding the use of dechlorinated water in freshwater aquatic toxicity tests.

A complete copy of the DERs (Data Evaluation Records) and review of the ecotoxicity studies(67 volumes) are enclosed for your records.

The product mentioned above has not passed the chemical screen; however, based upon our agreement to initiate a review of all submitted data, except toxicity data due to missing studies, data reviews are still being processed.

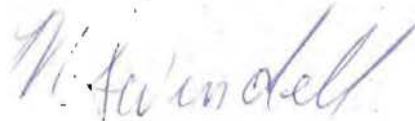
As per our letter of March 18th, 2003, due to the unusual circumstances associated with this new active ingredient, the Agency will place the environmental and ecological effects data as well as the chemistry and end-use application into review in the absence of a complete data package. Normally, a new active ingredient submission must be a complete package before the Agency will start its review process.

Please note that when toxicology data are submitted they will be placed into review on a track independent of the environmental and other reviews.

The product may not be lawfully distributed interstate commerce until the above discrepancies have been fulfilled.

If you have any questions concerning this letter, please contact Karen M. Leavy-Munk at (703)-308-6237.

Sincerely,

A handwritten signature in blue ink, appearing to read "M. Swindell".

Marshall Swindell
Product Manager 33
Regulatory Management Branch I
Antimicrobial Division(7510C)



January 19, 2004

Mr. Marshall Swindell
Product Manager Team 33
U.S. Environmental Protection Agency
Office of Pesticide Programs
Antimicrobial Division (7510W)
Regulatory Management Branch II
1921 Jefferson Davis Highway
Arlington, VA 22202-4501

SUBJECT: ECONEA™ Technical (43813-ET)
Response to EPA letter of August 26, 2003

Dear Mr. Swindell:

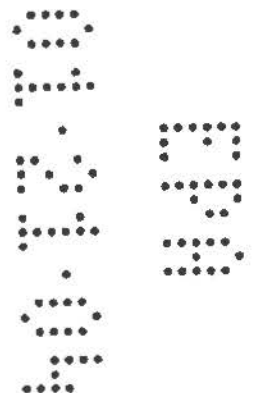
Referring to your letter of August 26, 2003, labeling amendments are proposed 1) to provide the formulator with more specific use directions covering application methods, use rates and equipment and 2) to revise the precautionary statements per FIFRA guidance for Toxicity Category I products, specifically the addition of clear statements for Personal Protective Equipment (PPE). The revised labels (6 copies) for ECONEA Technical are enclosed.

Additionally, EPA requested additional human exposure information related to using the Manufacturing Use Product (MUP) to formulate antifouling paint. This, however, is inconsistent with the August 4, 2003 Memorandum from Doreen Aviado, that accompanied the letter, which concluded that "Human exposure data provided by Janssen Pharmaceutica Inc. on the industrial paint formulation process and the screening level assessments on occupational exposure (MRID 45674128) are acceptable and satisfy data requirements under Series 875 Guidelines". At our meeting on November 5, 2003 to clarify this discrepancy, it was determined that the letter was in error, and that no additional occupational or post-application information was required at this time.

If any further follow-up is necessary at this time on labeling, please contact me.

Sincerely,

William R. Goodwine
Senior Director
Plant & Material Protection Division
(609) 730-2607





UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Mr. Bill Goodwine
Janssen Pharmaceutica, Inc.
11215 Trenton-Harbourton Road
Titusville, NJ 08560

Subject: ECONEA Technical
EPA File Number 43813-ET
Your Application Dated March 27th, 2003
EPA Received Date March 28th, 2003

The application referred to above, submitted in connection with registration under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, is incomplete.

Upon conducting a new chemical screen on the submitted materials for the intended use pattern and the following comments apply:

The nine studies provided for the product chemistry DER included most of the information required by the Group A and B, Series 830 Guidelines. Ten characteristics of the test substance, required by the guidelines, were not provided in the study Reports, including: (1) Description of Formulation Process, (2) Oxidation /Reduction: Chemical Incompatibility, (3) Flammability/ Flame Extension, (4) Explodibility, (5) Miscibility, (6) Corrosion Characteristics, (7) Dielectric Breakdown Voltage, (8) Viscosity, (9) Boiling Point/Boiling Range, (10) Particle Size, Fiber Length and Dimeter Distribution and are not required for this TGAI powder.

The data are adequate to support registration of the TGAI.

A complete copy of the science memo is enclosed for your records.

The product mentioned above has not passed the chemical screen; however, based upon our agreement to initiate a review of all submitted data, except toxicity data due to missing studies, data reviews are still being processed.

As per our letter of March 18th, 2003, due to the unusual circumstances associated with this new active ingredient, the Agency will place the environmental and ecological effects data as well as the chemistry and end-use application into review in the absence of a complete data package. Normally, a new active ingredient submission must be a complete package before the Agency will start its review process.

Please note that when toxicology data are submitted they will be placed into review on a track independent of the environmental and other reviews.

The product may not be lawfully distributed in interstate commerce until the above discrepancies have been clarified.

If you have any questions concerning this letter, please contact Karen M. Leavy-Munk at (703)-308-6237.

Sincerely,

Marshall Swindell
Product Manager 33
Regulatory Management Branch I
Antimicrobial Division(7510C)

Home
10-3-03



Date: 4/19/04

SUBJECT: Ecomea Ecotoxicity Studies Submitted in Support of Antifoulant Paint Use

DP Barcodes: 289026, 290345, 292015
PC Code: 119093

FROM: Richard C. Petrie, Team 3 Leader, Agronomist
Kathryn Montague, Biologist
OPP/AD/RASSB
Antimicrobial Division (7501C)

THRU : Norm Cook.
Chief, RASSB
Antimicrobial Division (7501C)

TO: Marshall Swindell, RM 33
Antimicrobial Division (7501C)

The RASSB has reviewed ecotoxicity studies submitted in support of chlorfenapyr (Ecomea) registration as an antifoulant paint. Numerous aquatic animal, plant and whole sediment toxicity tests were submitted for the active ingredient R107894, the first primary degradate CL 322,250, and two additional degradates CL322,248 and CL 325,195. A total of 67 studies were reviewed. See the "Status/Results of Submitted Ecomea Ecological Effects Studies - 4/13/04" below:

Status/Results of Submitted Econe Ecological Effects Studies

Econe Technical (R107894, AC303,268)

Study	Species	MRID	Status	Results
Avian acute oral	bobwhite	434928-09	Core	LD50 = 24.7, NOEL = 6 mg/kg
Avian acute oral	mallard	434928-08	Core	LD50 = 77, NOEL = 20 mg/kg
FW fish acute	bluegill	456740-02	Invalid	
FW fish acute	trout	456740-01	Invalid	
FW invert acute	daphnid	456740-04 457069-01	Invalid Invalid	
FW fish ELS	zebra fish	458939-01	Core	NOEC = 0.17 MATC = 0.25 ug/L
FW invert life cycle	daphnid	456740-08	Invalid	
ME fish acute	sheepshead	456740-03	Supplemental	LD50 = 23.71, NOEC = 10 ug/L
ME mollusk acute	E. oyster	456740-05	Supplemental	EC50 = 0.62, NOEC = 0.19 ug/L
ME invert acute	mysid	456740-06	Core	LD50 = 0.94 ug/L
ME fish ELS	Sheepshead	456740-07	Core	NOEC = 4.3, LOEC = 8.7 ug/L
ME invert lifecycle	mysid	456740-09	Supplemental	NOEC = 0.25, MATC = 0.36 ug/L
Whole sediment, FW	<i>Hyaella</i>	456740-10	Core	LC50 = 2.2, NOEC = 1.0 mg ai/L
Whole sediment, ME	<i>Leptocheirus</i>	456740-11	Core	LC50 = 1.1, NOEC = 0.50 mg ai/L
Green alga	<i>Selenastrum</i>	456741-17	Supplemental	EC40 = 4.49, NOEC = 3.1 ug/L
Blue-green cyanobacteria	<i>Anabaena</i>	458939-02	Core	EC50 = 350, NOEC = 9.2 ug/L
FW diatom	<i>Navicula</i>	458939-03	Core	EC50 = 5.5, NOEC = 0.99 ug/L
ME diatom	<i>Skeletonema</i>	456741-18	Supplemental	EC50 = 2.88, NOEC = 0.54 ug/L
Seedling emergence	Rice	456741-15	Core	<25% inhib at 170 ug/L
Duckweed	<i>Lemna g.</i>	456741-16	Core	EC50 = 87.2, NOEC = 22.0 ug ai/L

Major Degradate, CL 322,250

Study	Species	MRID	Status	Results
FW fish acute	bluegill	456740-23	Invalid	
FW fish acute	trout	456740-22	Invalid	
FW invert acute	daphnid	456741-02 457069-03	Supplemental Supplemental	LD50 = 0.65, NOEC <0.43 mg/L LD50 = 1.57 mg/L
FW fish ELS	zebra fish	456741-05	Invalid	
FW invert life cycle	daphnid	456741-07	Invalid	
ME fish acute	sheepshead	456741-01	Supplemental	LD50 >0.95, NOEC = 0.95 mg/L

ME mollusk acute	<i>E. oyster</i>	456741-03	Core	EC50=0.31, NOEC=0.046 mg/L
ME invert acute	mysid	456741-04	Core	LD50 = 0.57, NOEC , 0.41 mg/L
ME fish ELS	Sheepshead	456741-06	Core	NOEC = 0.24, MATC = 0.35 ug/L
Whole sediment, FW	<i>Hyalella</i>	456741-08	Core	LC50 = >35.0, NOEC = >35.0 mg ai/L
Whole sediment, ME	<i>Leptocheirus</i>	456741-09	Core	LC50 = >70.0, NOEC = >70.0 mg ai/L
Green alga	<i>Selenastrum</i>	456741-23	Supplemental	EC40 > 4.54, NOEC = 1.15 mg/L
Blue-green cyanobacteria	<i>Anabaena</i>	458939-07	Supplemental	EC50 > 0.83, NOEC = 0.83 mg/L
FW diatom	<i>Navicula</i>	458939-08	Supplemental	EC50 > 0.93, NOEC=0.93 mg/L
ME diatom	<i>Skeletonema</i>	456741-24	Supplemental	EC50 = 1.14, EC05 = 0.18 mg/L
Duckweed	<i>Lemna g.</i>	456741-22	Supplemental	EC50 = >0.99, NOEC = 0.53 mg ai/L

Minor Degradate, CL325, 195

Study	Species	MRID	Status	Results
Avian acute oral	bobwhite	444526-11	Core	LD50 = 741, NOEC = 192 mg/kg
Avian acute oral	Mallard	444526-12	Core	LD50 > 2250, NOEC = 2250 mg/kg
FW fish acute	bluegill	444526-17	Invalid	
FW fish acute	trout	456740-01	Invalid	
FW invert acute	daphnid	444526-18	Invalid	
		457069-02	Supplemental	LD50 = 3.57 ug/L
FW fish ELS	zebra fish	456740-16	Invalid	
FW invert life cycle	daphnid	456740-18	Invalid	
ME fish acute	sheepshead	456740-13	Supplemental	LD50 >16, NOEC = 16 mg/L
ME mollusk acute	<i>E. oyster</i>	456740-14	Core	EC50>14, NOEC=6.9 mg/L
ME invert acute	mysid	456740-15	Core	LD50 = 12.0, NOEC = 10.0 mg/L
ME fish ELS	Sheepshead	456740-17	Core	NOEC = 1.3 MATC = 1.9 mg/L
Whole sediment, FW	<i>Hyalella</i>	456740-19	Supplemental	LC50 = >49.0, NOEC = 49.0 mg ai/L
Whole sediment, ME	<i>Leptocheirus</i>	456740-20	Core	LC50 = >27.0, NOEC = >27.0 mg ai/L

Green alga	<i>Selenastrum</i>	456741-20	Supplemental	EC50=0.44, EC05 = 0.23 mg/L
Blue-green cyanobacteria	<i>Anabaena</i>	459452-01	Core	EC50= 6.5, NOEC = 1.40 mg/L
FW diatom	<i>Navicula</i>	458939-06	Core	EC50= 1.51, NOEC=0.85 mg/L
ME diatom	<i>Skeletonema</i>	456741-21	Supplemental	EC50 = 0.47, NOEC<0.28 mg/L
Duckweed	<i>Lemna g.</i>	456741-19	Core	EC50 = 13.0, NOEC = 5.9 mg ai/L

Additional Degradate, CL 322,248 (not found in fate studies)

Study	Species	MRID	Status	Results
FW fish acute	bluegill	456741-11	Invalid	
FW fish acute	trout	456741-10	Invalid	
FW invert acute	daphnid	456741-12	Supplemental	LD50 = 16.8 mg/L
FW invert life cycle	daphnid	456741-13	Supplemental	NOEC, 1.37, MATC = 3.85 mg/L
Whole sediment, FW	<i>Hyalella</i>	456958-04	Supplemental	LC50 = >49.0, NOEC = 49.0 mg ai/L
Whole sediment, ME	<i>Leptocheirus</i>	456741-14	Core	LC50 = >75.0, NOEC = >75.0 mg ai/L
Green alga	<i>Selenastrum</i>	456741-26	Supplemental	EC40 > 1.99, NOEC = 1.99 mg/L
Blue-green cyanobacteria	<i>Anabaena</i>	458939-04	Supplemental	EC50 > 1.0, NOEC = 1.0 mg/L
FW diatom	<i>Navicula</i>	458939-05	Supplemental	EC50 > 0.98, NOEC=0.98 mg/L
ME diatom	<i>Skeletonema</i>	456741-27	Supplemental	EC50 = 1.20, NOEC=0.16 mg/L
Duckweed	<i>Lemna g.</i>	456741-25	Supplemental	EC50 = >0.93, NOEC = 0.93 mg ai/L

The following table lists outstanding ecotoxicology studies. RASSB had determined that due to rapid degradation of R107894 to CL322,250 many of the acute and chronic toxicity tests must be repeated (invalid or supplemental ratings). Fish and oyster BCF's are also required for these two chemicals. The CL322-248 degradate, which is the debrominated form of CL322,250 found under anaerobic conditions and in saltwater, is a toxicity concern as well.

Further, bromine released during the degradation process must be characterized by the registrant. A significant amount of bromine could be toxic to aquatic plants and animals and may necessitate ecotoxicity testing for risk assessment.

Econea - Outstanding Eco Effects Data

Econea Technical (aka R107894, AC303,268)

Study	Species	Status
Avian dietary - 850.2200	bobwhite	Reserved
Avian dietary - 850.2200	mallard	Required
FW fish acute - 850.1075	bluegill	Required
FW fish acute - 850.1075	trout	Required
FW invert acute - 850.1010	daphnid	Required
FW invert life cycle - 850.1300	daphnid	Required
Fish BCF - 850.1730	bluegill	Required
Oyster BCF - 850.1710	E. oyster	Required
Green Algae - 850.5400	<i>Selenastrum capricornutum</i>	Required
Marine diatom - 850.5400	<i>Skeletonema costatum</i>	Required

Major Degradate, CL 322,250

Study	Species	Status
Avian acute oral - 850.2100	mallard	Required
Avian dietary - 850.2200	bobwhite	Reserved
Avian dietary - 850.2200	mallard	Required
FW fish acute - 850.1075	bluegill	Required
FW fish acute - 850.1075	trout	Required
FW invert acute - 850.1010	daphnid	Required
FW fish ELS - 850.1400	zebra fish	Required
FW invert life cycle - 850.1300	daphnid	Required
ME fish acute - 850.1075	sheepshead	Required
ME invert lifecycle - 850.1350	mysid	Required
Fish BCF - 850.1730	bluegill	Required
Oyster BCF - 850.1710	E. oyster	Required
Marine diatom - 850.5400	<i>Skeletonema costatum</i>	Required

Degradate, CL 322,248 (de-brominated CL322,250 - found in saltwater and anaerobic conditions)

Study	Species	MRID
Avian acute oral - 850.2100	mallard	Required
Avian dietary - 850.2200	bobwhite	Required

Avian dietary - 850.2200	mallard	Required
ME fish acute - 850.1075	sheepshead	Required
ME mollusk acute - 850.1025	E. oyster	Required
ME invert acute - 850.1035	mysid	Required
ME fish ELS - 850.1075	Sheepshead	Required
ME invert lifecycle - 850.1350	mysid	Required

See current OPP policy regarding use of dechlorinated water in freshwater aquatic toxicity tests below.

**U. S. ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460**

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

DATE: September 10 , 1999

SUBJECT: Use of dechlorinated water in freshwater aquatic toxicity tests

FROM: The Aquatic Technical Team
Environmental Fate and Effects Division

THROUGH: Aquatic Technical Team Co-chairs
Thomas M. Steeger, Fishery Biologist
Brian Montague, Fishery Biologist

TO: Mary Frankenberry, Chairperson
Science Policy Panel
Environmental Fate and Effects Division

The Aquatic Biology Technical Team (ABTT) has reviewed the issues regarding the use of dechlorinated water in freshwater aquatic toxicity tests and believes that it is necessary to recommend a consistent policy in EFED regarding studies that use dechlorinated water. Currently there is inconsistency in the classification of aquatic toxicity tests where dechlorinated water has been used; e.g., some scientists reject the study, whereas others accept the study with admonishment against its use in testing. The purpose of this memo is to clarify EFED policy

on the use of dechlorinated water in aquatic laboratory testing, both acute and chronic and thereby establish consistency among scientists in the handling of studies where dechlorinated water is used. Regardless of whether the test species is fish, macroinvertebrates or amphibians, if dechlorinated water is used in aquatic toxicity tests, it must be shown that first instar daphnids can survive unencumbered in the test water for 48 hours without food; otherwise, residual chlorine must be measured to demonstrate that it falls below specific levels. If a study fails to comply with these criteria, it should be classified as invalid since the effects of residual chlorine could not be dismissed.

It is generally recognized that chlorine-produced oxidants are toxic to aquatic animals. Chlorinated water should not be used in aquatic testing because the process of dechlorination is often incomplete. EPA's **1994 Reregistration Rejection Rate Analysis** states the Agency strongly recommends against the use of dechlorinated water, and that if its use cannot be avoided then the biological responses for the control organisms **and** chemical analyses must meet acceptable criteria (undefined in document). **ASTM E 729 -88a** (Standard Guide for Conducting Acute Toxicity Tests With Fishes, Macroinvertebrates, and Amphibians; 1989) states that if dechlorinated water is used, either (a) it must be shown that a sensitive aquatic species will survive, grow, and reproduce acceptably in it, **or** (b) it must be shown at least three times each week on nonconsecutive days that in fresh samples of dilution water either (1) *Acartia tonsa*, mysids (less than 24-h post release from the brood sac), bivalve mollusc larvae, or daphnids (less than 24-h old) do not show more signs of stress, such as discoloration, unusual behavior, or death, when held in water for at least 48 h without food than when similarly held in water that was not chlorinated and dechlorinated, **or** (2) the concentration of residual chlorine in fresh water is less than 11 ug/l or the concentration of chlorine-produced oxidants in salt water is less than 7.5 ug/l. EPA's **1975 publication** (EPA-660/3-75-009; Methods for Acute Toxicity Tests With Fish, Macroinvertebrates, and Amphibians) states "If a dechlorinated water is used, at the beginning of STATIC tests and daily during FLOW-THROUGH tests either it must be shown that first instar daphnids can survive in it for 48 hours without food or residual chlorine must be measured."

It is clear from the preceding discussion that either residual chlorine levels must be documented or toxicity tests on daphnids must be conducted to establish that chlorine residues had no effect. Failure to comply with these testing requirements if dechlorinated water is in use, would confound efforts to distinguish between what may be treatment effects and effects due to residual chlorine. In cases where dechlorinated water was used and the recommended tests regarding the effects of residual chlorine were not performed, the Aquatic Biology Technical Team recommends that the study be classified as invalid.



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Mr. Bill Goodwine
Janssen Pharmaceutica, Inc.
1125 Trenton-Harbourton Road
Titusville, NJ 08560-0200

Subject: ECONEA Technical
EPA File Symbol 43813-ET
Your Submission Dated September 30th, 2002
EPA Received Date October 3rd, 2002

The submission referred to above, submitted in connection with registration under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended, as per your rebuttal letter regarding the bridging of toxicology data for chlorfenapyr to the metabolite, CL303268, to support the registration of CL 303268 as an active ingredient in the antifouling paint product, "Sigma Nexxium 20 Antifouling and the technical material (ECONEA antifouling preservative), is unacceptable.

Upon review of the bridging toxicology data for the parent compound chlorfenapyr to address the toxicity of the CL303268 metabolite, the Agency has determined that it is incomplete. There is not enough submitted toxicity data for the CL 303268 metabolite to establish whether there is any concordance in toxicity between the parent, chlorfenapyr, and the metabolite (CL303268).

The proposed mode of action for the CL303268 metabolite is NOT entirely reflective of the toxicity of chlorfenapyr. Since there is a lack of concordance in the toxicity between chlorfenapyr and CL303268 metabolite and lack of data for two compounds demonstrating any concordance, the Agency has determined that the submitted toxicity database for chlorfenapyr does not support the registration of the CL 303268 metabolite.

Therefore, the Agency requests the submission of the following studies, a 90-day oral toxicity with neurotoxicity endpoints included in the study design, a developmental toxicity study in a rat, and a mutagenicity study battery, to better establish the relationship of the CL 303268 metabolite to chlorfenapyr.

The findings of the actual review will not be complete without a full battery of toxicity data.

A complete copy of all the science memos are enclosed for your records

The product mentioned above has failed the new chemical screen. The data will not be put into review until the above discrepancies have been clarified.

If you have any questions concerning this letter, please contact Karen M. Leavy-Munk at (703)-308-6237.

Sincerely,

Marshall Swindell
Product Manager 33
Regulatory Management Branch I
Antimicrobial Division(7510C)



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Mr. William Goodwine
Janessen Pharmaceutica, Inc.
11215 Trenton-Harbourton Road
Titusville, JN 08560

Subject: ECONEA Technical
EPA File Symbol 43818-ET
Your Application Dated April 12th, 2002
EPA Received Date May 2nd, 2002

The application referred to above, submitted in connection with registration under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended, is unacceptable for the following reasons:

Upon the conducting a new chemical screen on, ECONEA, the following deficiencies have been determined.

CHEMISTRY

The following studies were missing from the initial submission of data to support the chemical screen.

- a) 830.6317 Storage and Stability Study- It was stated that the technical is stable for five years. The Agency is requesting a study to support this claim.
- b) 830.6320 Corrosion Characteristics Study- The product information sheet states that the chemical is non-corrosive. The Agency is requesting a study to support this claim.

TOXICITY

The bridging data are insufficient to support the claims that the insecticide action of chlorfenapyr

is due to uncoupling of oxidative phosphorylation by the CL 303268 metabolite of chlorfenapyr. Therefore, the toxicology data for chlorfenapyr cannot be used to support hazard identification for the metabolite.

These are the issues that need to be addressed by the company before EPA can initiate any type of formal review of this data by the agency.

- 1) There are no data by the company to show that the CL 303268 metabolite is actually insecticidal by the proposed mode of action.
- 2) There are no submitted data the this metabolite ALONE is responsible for this mode of action (there are at least 5 metabolites of chlorfenapyr in mammalian studies sub-
- 3) There is no proof that any of the other metabolites of chlorfenapyr may or may not also work by this mode of action.
- 4) The disposition of the CL 303268 metabolite ay be quite different when administered directly compared to disposition of this metabolite when parent chemical is administered. The spectrum of toxicity of the metabolite may thus also be different.
- 5) Conduct of an acute oral toxicity study and a preliminary 28 day toxicity study with the CL 303268 metabolite is insufficient to make any claims supporting the mode of action.

Normally, to support toxicity claims between a parent chemical and a metabolite of that chemical, bridging data are submitted as one aspect of the data needed. The Office of Pesticide Programs requests a 90-day oral toxicity study, a developmental toxicity study, and at least one mutagenicity study as bridging data. These studies must be conducted according to the OPPTS harmonized test guidelines, Series 870. These data are necessary to determine if the spectrum of toxicity is the same between the parent chemical and the metabolite and to ger a reasonable idea of the relative potency of the toxicity of the compounds.

ECOLOGICAL EFFECTS

The submitted studies appear to be adequate for review and have passed the new chemical screen. However, pore water studies and avian reproductive studies may be requested once the data from the required studies are reviewed. These studies are reserved based on the findings from Tier II environmental studies.

ENVIRONMENTAL FATE

The submitted studies appear to be adequate for review and have passed the new chemical screen.

EXPOSURE

Human Exposure data requirements for MPs are not impeded by the Agency. However, the draft product labeling provided for ECONEA Technical is incomplete. Provide detailed information on the industrial mixing, loading and application processes, and any post-application worker (by stander) tasks anticipated when using this MP to formulate antifoulant paint end-use products.

Refer to the following human exposure data guidelines to develop this needed information:

GLN 875.1700 & 875.2700 Product Use Information

GLN 875.2800 Description of Human Activity

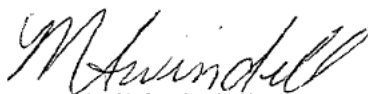
The findings of the actual review will not be complete without a full battery of toxicity data.

A complete copy of all the science memos are enclosed for your records.

The product mentioned above has failed the new chemical screen. The data will not be put into review until the above discrepancies have been clarified.

If you have any questions concerning this letter, please contact Karen M. Leavy-Munk at (703)-308-6237.

Sincerely,



Marshall Swindell

Product Manager 33

Regulatory Management Branch I

Antimicrobial Division(7510C)

 **Nader Elkassabany**

07/30/2002 11:26 AM

To: Karen Leavy/DC/USEPA/US@EPA
CC:
Subject: AC 303268 New Chemical Screen

FYI

----- Forwarded by Nader Elkassabany/DC/USEPA/US on 07/30/02 11:25 AM -----

 **Nader Elkassabany**

07/25/02 09:22 AM

To: Marshall Swindell/DC/USEPA/US@EPA
CC:
Subject: AC 303268 New Chemical Screen

Marshall,
This is Bob's part

----- Forwarded by Nader Elkassabany/DC/USEPA/US on 07/25/02 09:20 AM -----

Bob Quick

07/24/02 01:18 PM

To: Nader Elkassabany/DC/USEPA/US@EPA
cc: Norm Cook/DC/USEPA/US@EPA
Subject: AC 303268 New Chemical Screen

Norm and Nader-

Attached are comments on product chemistry for the new chemical screen conducted on 7/24/2002.

B.Q.



AC303268Screen.wpd

Inert ingredient information may be entitled to confidential treatment

New Chemical Screen AC 303268

Product Chemistry

I. Technical Product

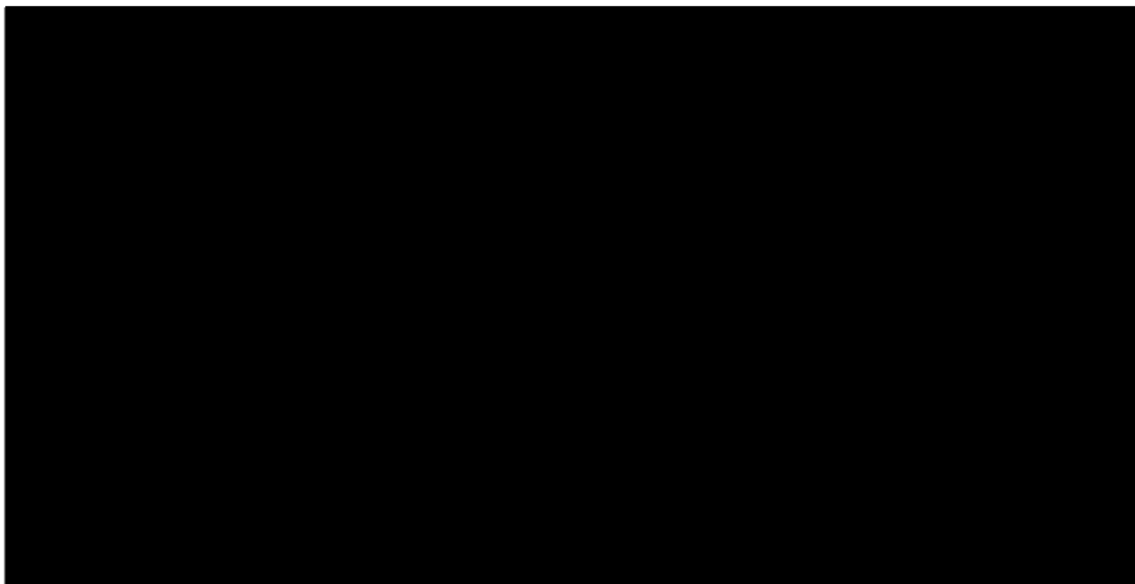
1. RASSB did not find the following studies in our screen of this submission:
 - a. 830.6317 Storage Stability Study. The registrant states that the technical chemical is stable for at least 5 years.
 - b. 830.6320 Corrosion Characteristics Study. The product information sheet states that the chemical is non-corrosive.

II. End Product

1. RASSB did not find the following studies in our screen of this submission:

The results are submitted for product chemistry studies on 830.7300, specific gravity and 830.6315, flammability but the individual studies are missing.
2. Inert Ingredients:

The following inert ingredients in the end product may not be cleared for use in pesticide formulations.



R. Quick



Wanda Jakob

07/25/2002 01:43 PM

To: Karen Leavy/DC/USEPA/US@EPA
cc: Doreen Aviado/DC/USEPA/US@EPA, Nader
Elkassabany/DC/USEPA/US@EPA
Subject: Re: Finds on the new chemical screen for the TGAI, ECONEA
Technical

Karen,

For the Eco portion, all required studies have been submitted for the parent compound and its metabolites. Industry should be aware that pore water studies and avian reproductive studies may be requested once we have reviewed the data from the required studies. The pore water and avian repro are reserved studies based on findings from first tier studies. An additional argument for these studies is based on the chemical strongly binding to the sediment and staying there. Invertebrates exposed to the chemical bound in the sediment are at a higher risk of exposure and those organisms getting into the food chain.

If you have any questions, let me know.

Regards,
Wanda

Wanda Jakob, Biologist
Antimicrobials Division/RASSB
Ariel Rios Building (7510C)
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460-0001
Phone: 703/308-6383
FAX: 703/308-8481
Karen Leavy

Karen Leavy

07/25/2002 12:39 PM

To: Nader Elkassabany/DC/USEPA/US@EPA, Wanda
Jakob/DC/USEPA/US@EPA, Doreen Aviado/DC/USEPA/US@EPA
cc:
Subject: Finds on the new chemical screen for the TGAI, ECONEA Technical

Hello,

If you could just forward a copy of your findings by e-mail to me, I would greatly appreciate it.
This will aid me in writing a response letter.

Thanks,
KML

SUBJECT: Input for the 7/24/02 New Chemical Screen Meeting on a new active ingredient (a.i.), **Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl)**, proposed for use as an antifoulant preservative. Occupational exposure considerations regarding the *Janssen Pharmaceutica Inc.* registration application for the 93.2 % a.i. manufacturing-use product (MUP) **ECONEA™ Technical** (EPA File Symbol 43813-ET); and Human Exposure Data requirements for the *Sigma Coatings USA* registration application for the 3.4 % a.i. use product (EP): **Sigma Nexxium 20 Antifouling** (EPA File Symbol 11350-GL) which also contains 3.4 % *Sea-Nine 211* as an a.i. co-biocide.

TO: Norm Cook, Chief
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

FROM: Doreen Aviado, Biologist
Team Two
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

THRU: Nader Elkassabany, Team Leader
Team Two
Risk Assessment and Science Support Branch (RASSB)
Antimicrobials Division (7510C)

DP
Barcode: D284099 (S617867)

Pesticide
Chemical(s)/ MUP: Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl) / 119093
No.(s): (R107894, or AC 303268, CL 303268)

EP: 2-(p-chlorophenyl)-3-cyano- 4-bromo-5-trifluoromethylpyrrole / 119093 and
4,5-dichloro-2-n-octyl-4-isothiazolin-3-one / 128101
(*Sea-Nine 211*, or C-9211, RH-287, or Kathon 287T)

MRID No.: 456741-28

PURPOSE:

The purpose for conducting this "new chemical screen" is three-fold:

1) To conduct a new chemical screen of materials provided by the registrant, *Janssen Pharmaceutica Inc.*, to Product Management Team 33 (PM 33) in support of a registration application for **ECONEA™ Technical** (EPA File Symbol 43813-ET), an MUP containing 93.2% of a new a.i., **Pyrrole-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl)** (R107894, I hard fouling organisms"; and

Product ingredient source information may be entitled to confidential treatment

2) To conduct a new chemical screen of materials jointly submitted by *Pharmaceutica Inc.* and the EP registrant *Sigma Coatings USA* to PM 33 in support of a registration application for the formulated paint product, **Sigma Nexxium 20 Antifouling** (EPA File Symbol 11350- GL), containing a co-biocide mixture of 3.4% of the new a.R107894 and 3.4% *Sea-Nine 211*; also

3) To decide if enough data have been provided in the registrant's submissions to facilitate putting the packages into RASSB review for assessing any applicable Human Exposure Data requirements needing to be addressed.

BACKGROUND:

In support of registration for **ECONEA™ Technical MUP**, as the a.i. technical source product, and the formulated **Sigma Nexxium 20 Antifouling** paint EP, *Janssen Pharmaceutica Inc.* and *Sigma Coatings USA* provided administrative materials including transmittal letters, product labeling and CSFs, meeting minutes, and data matrices citing studies conducted in support of the new active ingredient **Pyridine-3-carbonitrile, 4-bromo-2-(p-chlorophenyl)-5-(trifluoromethyl)** (aka R107894), as an alternative to TBTO in formulating antifoulant coatings.

Prior to submission of the registration applications, representatives of [REDACTED] (the a.i. manufacturer), *Janssen Pharmaceutica Inc.* (intended registrant of the technical source MUP), and *Sigma Coatings USA* (intended registrant of the formulated antifoulant paint EP) met with the Agency March 7, 2001 for a pre-application meeting to discuss data requirements for both the MUP and EP. Minutes from that meeting dated May 20, 2001 outline the following regarding human exposure data issues:

- Agency requested application/post-application information (data) in the form of a technical bulletin, product use information (MUP and EP), and description of human activities;
- "AD discussed possible submission of a 'human health exposure risk assessment' in lieu of conducting a dermal/inhalation exposure monitoring study once the Agency has reviewed the toxicity data and established toxicological endpoints."

Human exposure data were provided by *Janssen Pharmaceutica Inc.* in the form of an occupational exposure report (MRID 456741-28) dated January 11, 2002, entitled **Screening Level Occupational Exposure Assessments For R107894 (CL303268) As An Antifoulant In Paint Applied To Underwater Hulls**. This report supports the formulation **Sigma Nexxium 20 Antifouling** EP and appears to address potential occupational exposure concerns the Agency discussed with the registrant in the March 7, 2001 pre-application meeting. The submitted assessments are intended to qualitatively evaluate the potential worker exposures during shipyard painting operations and address, in a broad sense, the Human Exposure Data requirements under Series 875 Guidelines. As a conservative screening tool the assessment also includes quantitative dermal/inhalation exposure estimates and calculated MOEs for different painter scenarios (i.e., paint mixer/loader/applicator scenarios) based on surrogate data from PHED.

RECOMMENDATIONS: A new chemical screen was conducted on the submitted materials for the intended use pattern and the following comments apply:

ECONEA™ Technical (MUP containing 93.2% *R107894*):

- **FIFRA does not impose Human Exposure Data requirements for MUP's, only for typical EP's:** It is assumed that workplace safety standards set by OSHA for industrial manufacturing facilities and any specified personal protective equipment (PPE) are adequate to protect workers in contact with such chemicals;
- However, draft product labeling provided for **ECONEA™ Technical** is incomplete. Specific formulator use directions covering the application methods/use rates/equipment were not cited on the label nor provided in the form of a technical bulletin. Detailed information on the industrial processes used, and any post-application tasks performed by the industrial workers using this MUP is needed to better characterize any potential occupational exposure concerns once the application has been put into review. *Janssen Pharmaceutica Inc.* must provide detailed information on the industrial mixing/loading and application processes, and any post-application worker (bystander) tasks anticipated when using this MUP to formulate antifoulant paint end-use product **Sigma, Nexxium 20 Antifouling**. The registrant is encouraged to refer to the following human exposure data guidelines to develop this needed information:

GLN 875.1700 and 875.2700 Product Use Information
GLN 875.2800 Description of Human Activity

- As a note to the PM Team, the **ECONEA™ Technical** labeling Precautionary Statements will need revising according to FIFRA guidance for Toxicity Category I products which carry the DANGER signal word. Specifically, the addition of clear PPE statements for use of protective clothing and chemical-resistant gloves.

Sigma Nexxium 20 Antifouling (EP containing 3.4% *R107894* and 3.4% *Sea-Nine 211* as co-biocides):

- **The submitted data package was screened and can be put into review to support the EP:** Based on the new chemical screen of materials/data provided by the registrants *Janssen's* occupational exposure report (MRID 456741-28) submitted in support of the use of their *R107894* MUP in *Sigma's Sigma Nexxium 20 Antifouling* EP, is adequate to be put into full RASSB review for addressing in general the Human Exposure Data requirements under Series 875 Guidelines.

The data covered in the report will most likely fall under the minimum requirements for an EP (i.e., data to address GLN 875.1700 and 875.2700 *Product Use Information*, and GLN 875.2800 *Description of Human Activity* to better characterize the nature of the potential application/post-application exposures.) The quantitative exposure estimates in the report follows the Agency recommendation 'from a human health exposure risk assessment' cited in the May, 2001 meeting minutes as an alternative to generating any Application and/or Post-Application Guideline Studies under GLN 875.1100/GLN

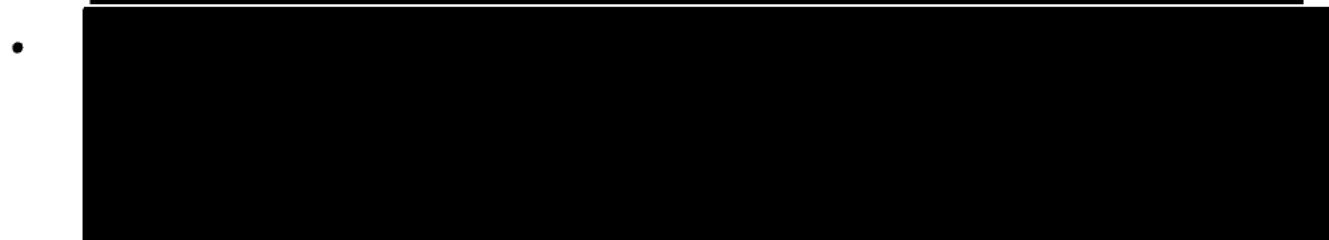
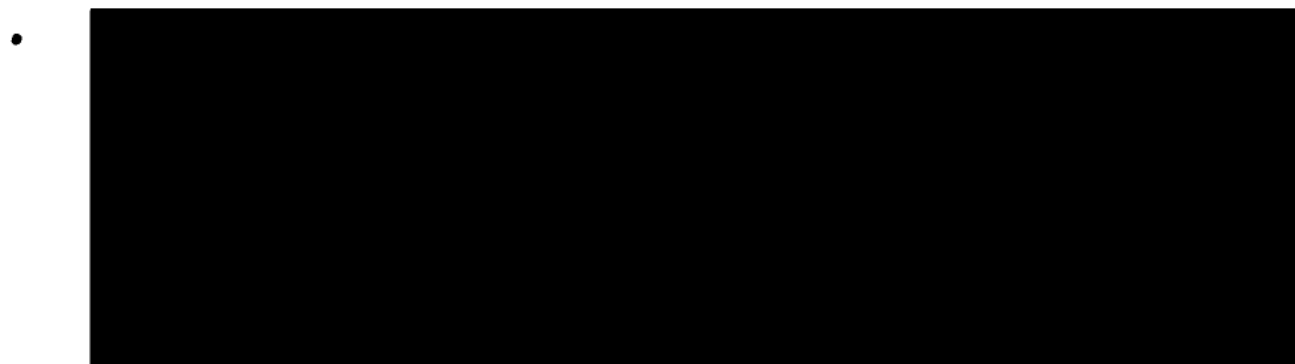
Inert ingredient information may be entitled to confidential treatment

875.1200 *Dermal Exposure Outdoor/Indoor* and GLN 875.1300/GLN 875.1400 *Inhalation Exposure Outdoor/Indoor*.

- **The Agency reserves the requirement for submission of specific Series 875 Guideline studies in support of the EP registration** No additional human exposure data is required at this time. A determination will be made after RASSB has been able to fully review the submitted data package (MRID 456741-28), characterize the toxicological hazards, select appropriate endpoints, and conduct an occupational exposure assessment.

The Agency requires registrants to address the Human Exposure Data guidelines for EPs when certain toxicity and exposure criteria are both met. In the case of **Sigma Nexxium 20 Antifouling**, the product appears to be of moderate toxicity (Toxicity Category III, CAUTION) yet the full toxicological characterization of the TGAI remains to be determined. However, the potential for dermal and inhalation exposure exists among mixers/loaders/applicators during occupational use and as post-application exposures to workers/bystanders reentering areas shortly after painting or in contact with wet paint during equipment clean-up.

- As a note to the PM Team, the submitted draft product labeling includes a technical bulletin which does not specify equipment and methods for application under "Instructions For Use". This information is needed.



- The complete Human Exposure Data requirements applicable to antifoulants are provided below for future reference.

Antimicrobial Use Category IX: Antifouling Coatings

Table 1. Human exposure data requirements - Application.

Data Requirements <u>Application</u>	Guideline Reference		I. Old Practice	II. Current Practice	III. Proposed for Subpart W
	Old	New			
Product Use Information	none	875.1700	NR	8R	8R
Dermal Exposure Outdoor	231	875.1100 875.1600	1CR	2CR	2CR

Dermal Exposure Indoor	233	875.1200 875.1600	1 ^{CR}	3 ^R	3 ^R
Inhalation Exposure Outdoor	232	875.1300 875.1600	1 ^{CR}	2 ^{CR}	2 ^{CR}
Inhalation Exposure Indoor	234	875.1400 875.1600	1 ^{CR}	3 ^R	3 ^R
Biological Monitoring	235	875.1500 875.1600	4 ^{CR}	4 ^{CR}	4 ^{CR}

Table 2. Human exposure data requirements - Post Application.

Data Requirements	Guideline Reference		I. Old Practice	II. Current Practice	III. Proposed for Subpart W
	Old	New			
<u>Post-application</u>					
Product Use Information	none	875.2700	NR	8 ^R	8 ^R
Description of Human Activity	133-1	875.2800	R	9 ^R	9 ^R
Indoor Surface Residue Dissipation	none	875.2300 875.2900	NR	NR	NR
Dermal Exposure	133-3	875.2400 875.2900	5 ^{CR}	6 ^R	6 ^R
Inhalation Exposure	133-4	875.2500 875.2900	5 ^{CR}	6 ^R	6 ^R
Biological Monitoring	235	875.2600 875.2900	7 ^{CR}	7 ^{CR}	7 ^{CR}

CR = Conditionally Required,

NR = Not Required,

R = Required.

Additional guidance is provided to data submitters as Guideline Reference No. 875.1600: Application Exposure Monitoring Data Reporting, and Guideline Reference No. 875.2900: Exposure and Risk Assessment Calculations.

FOOTNOTES:

¹ Application data are conditionally required when 1) based on the pesticide's toxicity certain toxicological criteria are triggered such as: Acute Toxicity Studies indicate Toxicity Category I for acute dermal and/or inhalation toxicity; and 2) the human activities associated with the pesticide use pattern can lead to potential adverse exposures to handlers (mixers/loaders/applicators).

² Required for outdoor uses when that is the primary use site, or if outdoor uses are expected to result in greater exposure than indoor uses.

³ Required to evaluate exposure to handlers for each intended antifouling coatings use pattern: antifouling paints for 1) boat hulls/boat bottoms, 2) crab/lobster pots, and 3) underwater structures/equipment (including fish farm structures/equipment).

^{4, 7} Biological monitoring may be substituted in addition to or instead of dermal/inhalation exposure data, provided adequate pharmacokinetics data are available to interpret the biological monitoring data. Post application biological monitoring is required in cases where passive dosimetry techniques are not applicable for a particular exposure scenario, for example (but not limited to), swimming pools, hot tub baths, and showering.

⁵ Post Application data are conditionally required when 1) based on the pesticide's toxicity certain toxicological criteria are triggered such as: Acute Toxicity Studies indicate Toxicity Category I or II for acute dermal and/or inhalation toxicity; and 2) the human activities associated with the pesticide use pattern can lead to potential adverse exposures to workers upon reentry, and/or bystanders and residents.

⁶ Testing for post application exposure is required to: 1) evaluate exposure to persons removing antifouling coatings from treated surfaces, such as boat hulls, if the activity is not covered by OSHA regulations, and 2) evaluate bystander inhalation exposure following application of antifouling coatings.

Measurements of indoor inhalation exposure may be combined with tests discussed in OPPTS 875.1400.

⁸ Product use information, where applicable, includes ranges and typical values for application rates, timing, methods, sites, frequency, equipment used, formulation types, and other relevant use data.

⁹ Descriptions of human activity include exposure time per activity, type of protective clothing worn, application sites, activity patterns, and other relevant use data.

**RESULTS OF NEW CHEMICAL SCREEN OF ECOTOXICOLOGY DATA
SUBMITTED FOR NEW ANTI-FOULANT (chlorfenapyr degradate):**

A total of 57 studies were reviewed. All studies were found acceptable for review.

Four of the 57 submitted studies have already been reviewed by EFED, leaving 53 studies for contractor review.

Studies were submitted for four different test materials:

R107894 (TGAI)
CL325.195 (TEP)
CL322.248 (TEP)
CL325.250 (TEP)

Summary of Studies Submitted:

Study Type	Number of Studies for Contractor - EFED Reviewed	
Fish acutes	10	1
Fish Early Life Stage	5	0
<i>Daphnia magna</i> acute	6	0
<i>Daphnia magna</i> chronic	4	0
Oyster acute	3	0
Mysid acute	3	0
Mysid chronic	1	0
Amphipod acute	8	0
Avian 14 day acute	0	2
Avian Oral LD50	0	1
Plant acute	13	0
	<hr/> 53	<hr/> 4

- No fish bio-accumulation studies referenced.
- No avian reproduction studies referenced.

***Daphnia magna* studies for chlorfenapyr degradates:**

48 Hour Acutes

MRID		Test Chemical		Passed Screen?		Contractor Review Needed?
45674004	-	R107894	-	YES	-	YES
45706901	-	R107894	-	YES	-	YES
45674102	-	CL322-250	-	YES	-	YES
45706903	-	CL322-250	-	YES	-	YES
45674112	-	CL322-248	-	YES	-	YES
45706902	-	CL325-195	-	YES	-	YES

Chronics

45674008	-	R107894	-	YES	-	YES
45674113	-	CL322-248	-	YES	-	YES
45674018	-	CL325-195	-	YES	-	YES
45674107	-	CL322-250	-	YES	-	YES

Fish studies for chlorfenapyr degradates:

96 Hour Acutes

Rainbow Trout:

45674001	-	R107894	-	YES	-	YES
45674012	-	CL325-195	-	YES	-	YES
45674110	-	CL322-248	-	YES	-	YES
45674022	-	CL325-250	-	YES	-	YES

Bluegill Sunfish:

45674002	-	R107894	-	YES	-	YES
45674021	-	CL325-195	-	YES	-	NO (EFED Review)
45674111	-	CL322-248	-	YES	-	YES
45674023	-	CL325-250	-	YES	-	YES

Sheepshead Minnow:

45674003	-	R107894	-	YES	-	YES
45674013	-	CL325-195	-	YES	-	YES
45674101	-	CL325-250	-	YES	-	YES

Fish Early Life Stage Studies:

MRID		Test Chemical		Passed Screen?		Contractor Review Needed?
Zebra Fish:						
45674007	-	R107894	-	YES	-	YES
45674105	-	CL322-250	-	YES	-	YES
45674016	-	CL325-195	-	YES	-	YES

**Sheepshead
Minnow:**

45674106	-	CL322-250	-	YES	-	YES
45674017	-	CL325-195	-	YES	-	YES

Eastern Oyster studies for chlorfenapyr degradates:96 Hour Acute Studies:

45674005	-	R107894	-	YES	-	YES
45674014	-	CL325-195	-	YES	-	YES
45674103	-	CL322-250	-	YES	-	YES

Mysid shrimp studies for chlorfenapyr degradates:96 Hour Acutes

45674006	-	R107894	-	YES	-	YES
45674015	-	CL325-195	-	YES	-	YES
45674104	-	CL322-250	-	YES	-	YES

Chronic

45674009	-	R107894	-	YES	-	YES
----------	---	---------	---	-----	---	-----

Avian Toxicity Studies for chlorfenapyr degradates:

Oral LD50 using soil metabolite

MRID???	-	CL325-195	-	YES	-	NO (EFED Review)
---------	---	-----------	---	-----	---	------------------

(Poor photocopy)

14 Day Acute Toxicity Feeding Studies:

MRID		Test Chemical		Passed Screen?		Contractor Review Needed?
Mallard duck						
43492809	-	R107894	-	YES	-	NO (EFED Review)
Bobwhite quail						
43492809	-	R107894	-	YES	-	NO (EFED Review)

Plant toxicity studies for chlorfenapyr degradates:

Aquatic macrophyte *Lemna gibba*

45674116	-	R107894	-	YES	-	YES
45674125	-	CL322-248	-	YES	-	YES
45674119	-	CL325-195	-	YES	-	YES
45674122	-	CL325-250	-	YES	-	YES

Green algae

45674117	-	R107894	-	YES	-	YES
45674126	-	CL322-248	-	YES	-	YES
45674120	-	CL325-195	-	YES	-	YES
45674123	-	CL325-250	-	YES	-	YES

Marine diatom

45674118	-	R107894	-	YES	-	YES
45674127	-	CL322-248	-	YES	-	YES
45674121	-	CL325-195	-	YES	-	YES
45674124	-	CL325-250	-	YES	-	YES

Rice seedling emergence

45674115	-	R107894	-	YES	-	YES
----------	---	---------	---	-----	---	-----

Whole Sediment Acute Toxicity Studies for chlorfenapyr degradates:

MRID	Test Chemical	Passed Screen?	Contractor Review Needed?
-------------	----------------------	-----------------------	----------------------------------

Amphipod *Hyaella azteca* 10 day acutes:

45674010	-	R107894	-	YES	-	YES
45674019	-	CL325-195	-	YES	-	YES
45695804	-	CL322-248	-	YES	-	YES
45674108	-	CL322-250	-	YES	-	YES

Amphipod *Leptocheirus plumulosus* 10 day acutes:

45674011	-	R107894	-	YES	-	YES
45674020	-	CL325-195	-	YES	-	YES
45674114	-	CL322-248	-	YES	-	YES
45674109	-	CL322-250	-	YES	-	YES